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CHRONIC EPIDEMIC ENCEPHALITIS

REPORT OF A CASE: CLINICAL RECORD, COMPLETE NECROPSY AND DETAILED HISTOLOGIC STUDY OF THE CENTRAL NERVOUS SYSTEM *

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SAN FRANCISCO

The following report of a case of epidemic encephalitis representing both clinical and anatomic examinations is of particular interest because of the persisting inflammatory brain changes after fourteen months, and also because complaints of abdominal pain, muscle spasm and gastric distress thought to be due to local causes ultimately led to an exploratory laparotomy. This exploration revealed no pathologic condition to account satisfactorily for the abdominal symptoms, and the final analysis of the case explained these symptoms as being due to brain lesions.

CLINICAL REPORT BY DR. SCHALLER

History.—K. G., dispensary number 91724, aged 42, an American laborer (harvest hand), was admitted to the clinical ward of Lane Hospital on Jan. 3, 1921. He complained principally of abdominal pain, but other complaints were: headache, burning pain in the back and legs, soreness over the lower part of the chest, numbness and weakness of the right arm, hoarseness and difficulty in swallowing, tinnitus and nervousness. The abdominal pain was described as gnawing in character, relieved for a short time by soda or by eating. Three or four times a day he had a severe jerking pain like stomachache, generally on the left side of the abdomen under the ribs, but also on the right side. He had been nauseated only once, about two months ago, but had never vomited. Occasionally he suffered with a sour stomach and burning regurgitation after eating. This had occurred more frequently of late. There was a tendency to constipation.

In September, 1920, he was in a hospital in Berkeley, Calif., for two weeks, where a diagnosis of gastric ulcer was made. He was not benefited by a special diet. He said that he weighed 125 pounds (56 kg.), his normal weight being 165 pounds (74 kg.).

The patient attributed his trouble to an illness he had had while in Nebraska in November, 1919, which began with roaring in the ears, sharp occipital headache and alternating chilly and feverish sensations. He thought he had grip. Following this onset he felt run down, and when he attempted to work he felt worse. He had constant dull headaches. One month after the beginning of

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his illness he was seized with convulsions which lasted about forty-eight hours, coming on one after another. They were intensely painful causing him to double up as with colic. These convulsions were described as a general spasm without loss of consciousness, and a part of the spasm seemed to be inside his abdomen. These spasms of pain terminated suddenly, leaving him weak, trembling and scarcely able to talk. He was removed to a hospital a day later where a diagnosis of ptomaine poisoning was made. Here he remained for four months, and he was said to have been delirious for two months. After regaining consciousness he was drowsy, resembling he thought, a patient in a neighboring bed whose case was diagnosed as lethargic encephalitis. The headaches persisted, and about a week after leaving the hospital a churning pain began in the stomach, his voice became hoarse, and a twitching in both arms and shoulders developed so that he could hardly use either. At times his muscles would contract involuntarily so as to jerk him violently one way or another. He improved until the latter part of 1920, difficulty of speech disappearing, and his left arm becoming normal. During the last few months, however, his condition had become aggravated gradually reaching the stage in which he had difficulty with speech and swallowing, and could use his right arm very little; his stomach trouble also increased.

He had acute inflammatory rheumatism when 7 years old, lasting three years, from which he recovered without complications, and the usual children's diseases, including diphtheria. "Chancres" eight years ago were treated locally. Gonorrhea was denied. He had smallpox several years ago.

The family history was unimportant.

Examination.—The patient was first examined in the medical service of Dr. A. W. Hewlett. The chest was well developed but asymmetrical due to thoracic scoliosis. The left side moved less posteriorly than the right. No abnormalities were found in the lungs. The heart impulse was not seen or felt, and the cardiac dimensions were of normal size. The heart sounds were clear. The heart rate was accelerated; the blood pressure was: systolic, 150; diastolic, 100. The abdomen was on a level with the ribs. The right side was quite rigid, particularly above; the left side moderately so. Repeated later examinations of the abdomen continued to show marked rigidity and muscle spasms, especially in the upper half and on the right side (upper right quadrant). The patient continued to complain of pain just beneath the ensiform.

Report of Eye Clinic (Albert B. McKee).—The fields and pupils were normal. Vision in the right eye was 20/100; with plus 2 hypermetropic astigmatism correction, vision was 20/40; vision in the left eye was 20/30-20/20; no glass. The backgrounds were normal. Diagnosis: Anisometropia (right hypermetropic astigmatism); double dacrocystitis.

Roentgen-Ray Examination.—The gastro-intestinal tract was normal. The chest was normal except for old pleural scars.

Report from the Ear, Nose and Throat Clinic (E. C. Sewall).—Pointing tests with the right arm were influenced by interference with movements caused by impaired muscular action. The left arm showed a slight spontaneous past pointing to the right. Past pointing after turning was in the proper direction but hypo-active. All canals responded properly to stimuli, except the left vertical canal, which showed a slightly perverted nystagmus after caloric stimulation of five minutes.

Ears: The ear drums were fibrous and retracted; poor light reflex.

Hearing of watch-tick was diminished in the right ear so that a watch-tick normally heard at a distance of 40 inches (101 cm.) could only be heard at 3 inches (7.6 cm.). In the left ear it could only be heard on contact. In the tuning-fork tests air conduction was good in both ears, but bone conduction was only fair. The Rinné test was positive. In the Weber test the vibrations were lateralized toward the right.

Neurologic Examination (Feb. 9, 1921).—General Survey: The patient was poorly nourished and weighed 125 pounds (56 kg.). He was nervous and trembling, and sweated profusely at the time of examination. A fine muscular tremor was present on both sides of the face and neck, most marked on the left side. The thyroid cartilage was drawn somewhat to the right. The Romberg sign was negative, and the gait was normal.

Coordination: A slight ataxia was present in the finger to nose test, with marked intention tremor. The heel to knee test was normal. The spread fingers showed a coarse tremor. An intention tremor was present when the patient attempted coordinate movements (reaching for a glass) under observation.

Neuromuscular: Twitchings (tremor) of facial and platysma muscles were present; there was a slight atrophy of the right platysma. The muscles of mastication seemed weak as a whole; there was marked atrophy of the left masseter and temporal muscles. The left pterygoids were involved (inability to move the jaw laterally to the right as far as to the left). The grip of the teeth was weak; the grip was weak in both hands, more marked in the right.

Reflexes: The tendon reflexes were hyperactive throughout. There were no pathologic pyramidal reflexes: the Babinski, Oppenheim and Gordon signs were negative.

Sensibility: Somatic sensation was unaffected by the usual tests for superficial and deep sensation.

Cranial Nerves: The first nerve was normal. Second Nerve: The fields and fundi were normal. (See special eye examination.) Third, Fourth and Sixth Nerves: The pupillary reactions and the eye movements were normal. A slight nystagmus was present to the left when looking to the left. There was no diplopia. Fifth Nerve: Taste on the anterior two thirds of the tongue was normal. The corneal reflex was present bilaterally. The muscles of mastication were weak, especially on the left side, as noted. Seventh Nerve: Tremor was present in the facial muscles, especially on the left and in the platysma. On emotional expression the face was less wrinkled on the right side than on the left. Eighth Nerve: See special ear examination. Ninth, Tenth and Eleventh Nerves: Some difficulty was experienced in swallowing, marked at times. Taste was normal on the posterior third of the tongue. The trapezius muscle was slightly atrophic on the right. Twelfth Nerve: There was slight deviation of the tongue to the left. There was some difficulty of protrusion of the tongue, but no tremors.

Laboratory Examination.—On Jan. 31, 1921, the urine was clear, yellow-amber, acid, 1.025; no abnormalities were found. Blood analysis on Feb. 1, 1921, showed 4,600,000 red cells, hemoglobin 85 per cent. (Talquist), white cells 6,050, polymorphonuclears 74 per cent., lymphocytes 20 per cent., large mononuclears 5 per cent., transitionals 1 per cent. A repetition of the white count on February 14 showed 7,350 cells. The sputum was examined on Feb. 1, 1921; it was whitish with a musty odor and in consistency was watery streaked with bright red blood. There was no tubercle bacilli, but streptococci were

abundant; there were also many staphylococci. A feces examination on Jan. 31, 1921, revealed a soft formed dark brown material with a few vegetable fibers and cells, and a few small particles of fat; the examination was otherwise negative. A cerebrospinal fluid examination was made on Feb. 5, 1921. Approximately 15 c.c. of fluid were withdrawn; the pressure was 90 mm. The fluid was clear in appearance and contained 1.2 leukocytes per cubic millimeter. The Nonne and Noguchi tests for globulin were negative, but the Pandy was faintly positive. The Wassermann reaction was negative in amounts as high as 1 c.c., cholesterinized beef heart antigen being used. The blood Wassermann test under date of Feb. 1, 1921, was negative with three different antigens—cholesterinized beef heart antigen, acetone insoluble antigen and guinea-pig heart antigen. Repeated tests of the stomach contents (five in all) from February 1 to February 13, inclusive, after the ingestion of an Ewald test meal, showed a total acidity ranging from 95 to 32. The free hydrochloric acid ranged between 74 and 25. There was no free blood found, and apparently digestion was fair.

Nurse's Record.—The temperature on admission was 99 F., but dropped to normal the next day. Several early morning temperatures of 97 were recorded in the following days. Rectal temperatures as high as 100-100.4 F., were noted on January 7, 9, 10, 11 and 12. The pulse on one occasion (February 11) was registered at 100, but averaged between 80 and 90. The respirations averaged 20.

A note on Feb. 16, 1921, stated that the patient had been on a Sippy diet for nine days and felt more comfortable, and that the muscle spasm was somewhat lessened, but the result was not striking. On Feb. 18, 1921, the patient was transferred to the surgical clinic for an exploratory abdominal operation.

Operation.—Feb. 19, 1921, an exploratory laparotomy appendectomy was performed. The operators were Dr. John F. Cowan, assisted by Dr. Frances Ford and Dr. Lloyd Reynolds. A high right rectus incision was made; the exploration revealed a normal stomach, gallbladder, liver, spleen and pancreas. Both kidneys were normal in size and position. The bladder and prostate appeared normal. There was no evidence of tubercles in the peritoneum, nor any enlargement of the retroperitoneal lymph glands. The appendix was atrophic and was removed in the usual manner. Nothing was found in the abdomen to account for the patient's symptoms. On Feb. 20, 1921, the patient vomited a considerable amount of dark coffee-ground material, which gave a positive benzidin test for blood. On February 22 there was great difficulty in swallowing, and fluids were regurgitated through the nose; a considerable heavy sputum apparently came from the throat. At 5 a. m. on February 23 the patient died.

Summary.—An American laborer, aged 42, developed symptoms in November, 1919, which were suggestive of a severe attack of epidemic encephalitis. Improvement was noted for a year, but at the end of this period there seemed to be a mild recurrence of certain of his former complaints, notably difficulty of speech and of swallowing, headache, generalized burning pains and nervousness. Added to these were more distressing local complaints of abdominal pain, muscle spasm and gastric distress, which finally led to an exploratory operation. Except for an atrophic appendix, which showed on removal microscopic evidence of a chronic obliterative process, no gross lesions were found. The patient died four days after the operation from bulbar paralysis.

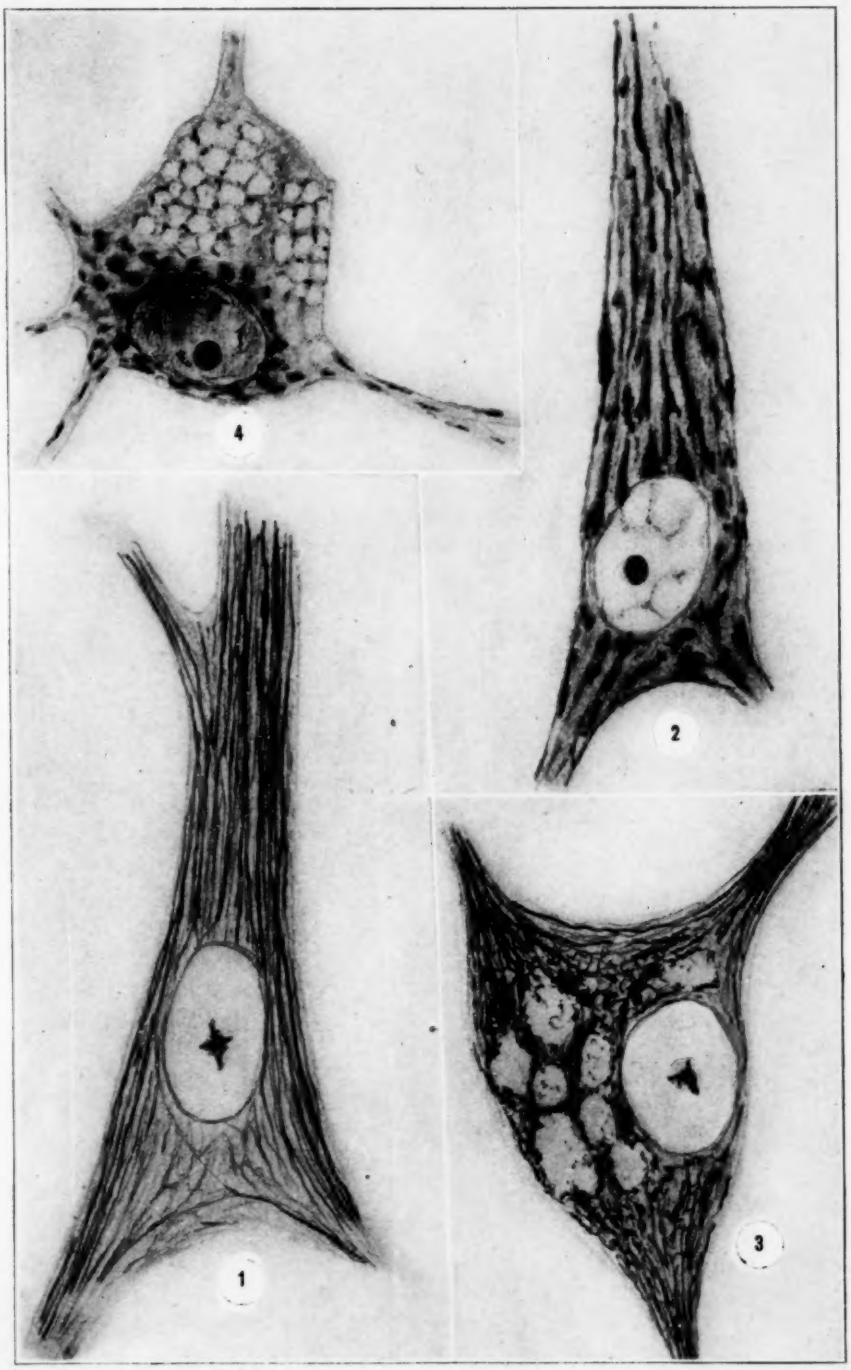

Plate 1.

Fig. 1.—Giant cell from cerebral cortex stained by Bielschowsky's method, showing normal fibrillae.

Fig. 2.—Similar cell from same region stained with methylene blue, showing normal tigroid bodies.

Fig. 3.—Ganglion cell from thalamus stained by Bielschowsky's method, showing vacuolization and marked degeneration of the intracellular fibrillae.

Fig. 4.—Similar cell from same region stained with methylene blue, showing degeneration of the tigroid bodies and the same vacuolization.

ANATOMIC REPORT BY DR. OLIVER

The necropsy examination was performed six hours after death. The body was that of a fairly strongly built, rather emaciated man of about 30 years.

The skull-cap and the external surface of the dura were normal. The superior longitudinal sinuses contained some postmortem clots. The pia over the convexity of the hemispheres showed a mild hyperemia and edema. The pia over the base of the brain was also hyperemic and showed a diffuse thickening around the sylvian fissure. There were no adhesions between the pia and the gray matter. There were a few arteriosclerotic plaques in the vessels at the base of the brain. A section through the brain stem at the pons was apparently normal. The lateral ventricles were not dilated. The large venous sinuses at the base of the brain contained some postmortem clots. The dura and the bone were apparently normal.

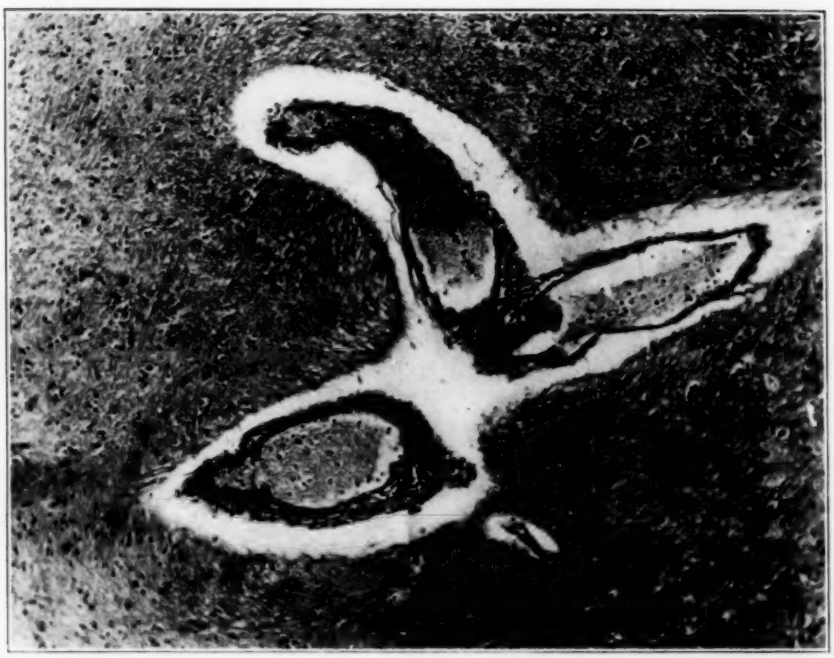

Fig. 1.—Small vessels in the thalamus, showing marked perivascular round cell infiltration.

Gross and microscopic examinations of the viscera were practically negative with the exception of the presence of bronchopneumonia.

After small pieces had been removed and fixed separately in different reagents, the brain was fixed *in toto* in 10 per cent. formaldehyd and was then cut in gross frontal sections. The only gross lesions noted in these sections were hyperemia and red spots which had the appearance of hemorrhages in the region of the substantia nigra.

Microscopic sections were prepared from various levels of the cervical cord, the brain stem, the basal ganglions, the cerebellum and the cerebral cortex, and stained with methylene blue, Bielschowsky's fibrillar stain, the Weigert-Pal method, Hamberger's Victoria blue method for glia, sudan III, van Gieson,

and hematoxylin and eosin. As the lesions encountered are more or less the same in different regions, a general description is first given followed by a topographical study. The lesions found in the more acute type of lethargic encephalitis are only briefly mentioned as they have been described repeatedly.

Lesions of Vessels.—The most striking change was a round cell infiltration around the smaller vessels in the adventitial tissue (Fig. 1). The cells found were those usually described, comprising lymphocytes, plasma cells and a few larger cells of the type of "endothelial leukocytes." No polymorphonuclear leukocytes or eosinophils were seen. Fat stains showed a moderate amount of fat in the form of coarse droplets in the larger type of cell.

Besides these more acute lesions, proliferative changes in the adventitial connective tissue were also present. These consisted in an increase in fusiform cells with large vesicular nuclei and intercellular collagen fibrils. In some regions the adventitia was distinctly thickened by this proliferation.

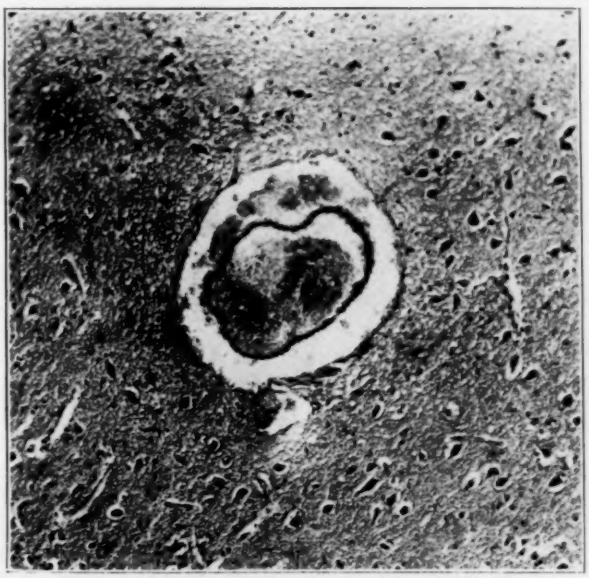

Fig. 2.—Small vessel in the thalamus, showing perivascular hemorrhage.

The other striking vascular lesion was hemorrhage. As a rule this consisted in extravasation of red cells into the perivascular tissues (Fig. 2). More rarely irregular infiltrations into the nervous tissue were found extending some distance from the vessel concerned. In all cases the red blood cells were well preserved so that the hemorrhages had apparently occurred late in the course of the disease.

Lesions in the Ganglion Cells.—Changes in the ganglion cells were studied with methylene blue stains and by Bielschowsky's method. As the cerebral cortex was entirely normal (Plate 1, Figs. 1 and 2), sections of this region served as a control for the staining of cells in the regions which showed abnormalities. Such a control is of importance, especially in using the Bielschowsky method, as it often produces artefacts.

The changes in the cells as studied with the methylene blue stains showed a great variety in types of lesions. Rarely Nissl's so-called "acute" type of degeneration was found. Such cells showed eccentricity of the nucleus and chromatolysis of the tigroid bodies, the process being more advanced as a rule in the neighborhood of the nucleus.

More commonly, however, the appearance was that usually considered typical of chronic degeneration. Some cells were small and shrunken, the chromatophile substance either condensed to an opaque irregular mass or in part dissolved. The nucleus, also shrunken and distorted, lay eccentrically and showed either pyknotic or karyolytic changes. Other cells presented only a shadowy outline of their former appearance.

Fig. 3.—Area of gliosis in thalamus, showing the nuclei of many astrocytes and many coarse glia fibrils.

With these changes there was in practically all the regions more severely involved, marked vacuolization of the protoplasm (Plate 1, Fig. 4). These vacuoles were filled with coarse granules, which remained a bright yellow in the blue protoplasm of the cells, and in sections stained for fat, presented a deep reddish-yellow color.

Satellitosis was commonly seen as well as definite neuronophagia. The shadow forms especially were often filled with deeply staining nuclei.

The Bielschowsky preparations showed a normal appearance in the cells of the cerebral cortex (Plate 1, Fig. 1), and as all the tissues were fixed in the same fluid and all run through the staining process at the same time, the changes described in other regions may be considered as actual.

Whereas the intracellular fibrillae of the pyramidal cells were clearly outlined throughout the entire length of the cells and its processes, in those cells which showed abnormalities with the methylene blue stain, striking changes were seen. In many cases the fibrillae of the cell processes, dendrites and axons, were fairly well preserved. At their entrance into the cell body, however, they rapidly lost their normal direction, became involved in an entangled network and ultimately were broken up into fine granules which continued for some distance in the general direction of the fibril from which they arose. Other cells, fewer in number, showed a complete loss of fibrillae in their central portions, which were completely filled with finely granular material. In those cells in which vacuolization has occurred, the fibrillae, besides showing

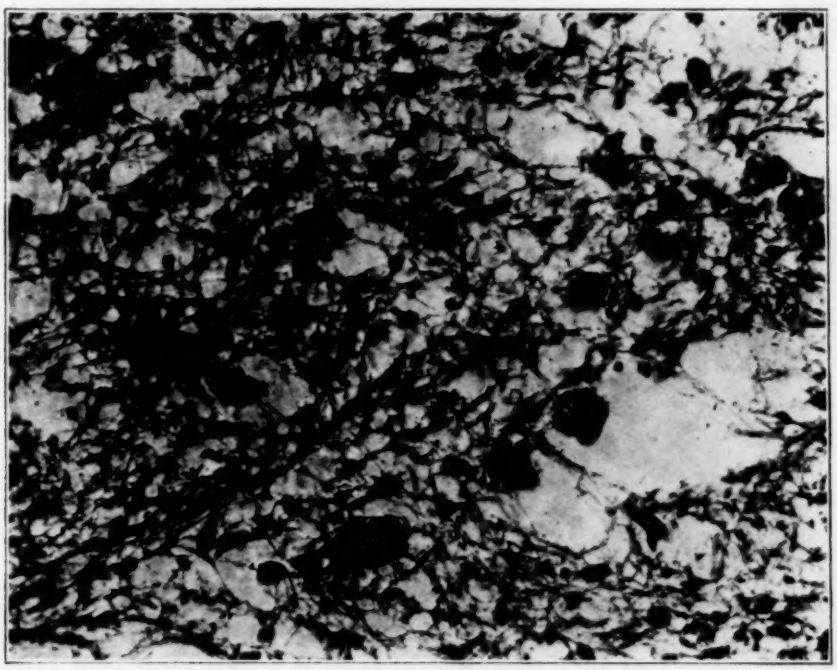

Fig. 4.—Area of spongy gliosis from the nucleus of the ala cinerea.

granular degeneration, were compressed between the clear spaces and were thus heavily outlined in dense black by the reduced silver (Plate 1, Fig. 3). As the vacuoles increased in size this disarrangement of the fibrillae continued until nothing remained except deeply stained fragments and granules densely compressed between the large vacuoles.

Changes in the Neuroglia.—The glia in the regions more severely affected showed definite evidence of proliferation. This consisted in the presence of an excessive number of large cells of the astrocyte type as well as a marked increase in the glia fibrils (Fig. 3). Such proliferation was often found in those nuclei whose ganglion cells showed marked lesions. In such areas of gliosis it was not uncommon to find the fibrils widely separated and so forming a coarse network with clear intervening spaces. The fibrils in such regions were so coarse that they stained well with the picric acid of the van Gieson mixture (Fig. 4).

In many of the areas of glial proliferation were large numbers of amylaceous bodies (Fig. 5). These structures had the usual opaque appearance that is commonly seen in them when occurring in those chronic processes which are accompanied by atrophy of the nerve elements and compensatory gliosis.

In spite of this marked proliferation of the fixed glia, ameboid cells or "Gitterzellen" were rarely seen.

Lesions in the Nerve Roots.—The roots of all the cranial nerves were examined and lesions found in several. These were of the same type as those found in the internal portions of the central nervous system, and consisted of round cell infiltration around small vessels and perivascular hemorrhages

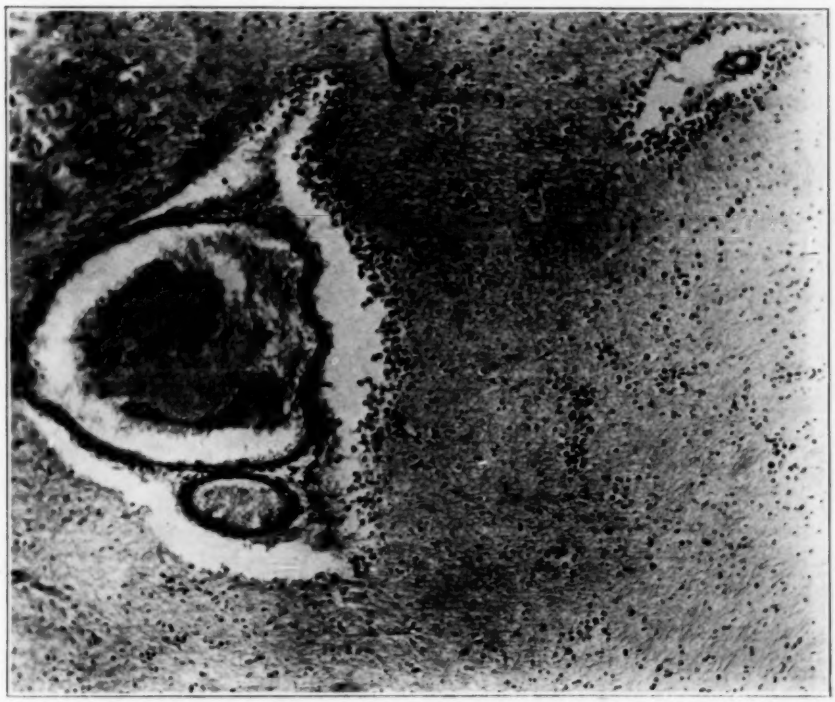

Fig. 5.—Collections of amylaceous bodies around vessels in the subthalamic region.

(Fig. 6). Evidences of chronic processes were also seen, such as increase of glia nuclei and fibrils and the presence of large numbers of amylaceous bodies. These lesions were often most intense at the exit of the nerve roots through the pia.

Lesions in the Myelinated Tracts.—No marked degeneration of any of the long tracts of the brain stem were found. The radial fibers of the cerebral cortex also showed no severe lesions. With the high power lens one could find, however, in practically all regions slight irregularities in the myelinated fibers.

Lesions in the Pia-Arachnoid.—Over the base of the brain, pons and medulla there was a slight increase in the cells of these membranes, consisting in the most part of lymphocytes. As has already been mentioned, these changes were

likely to be most marked at the exit of cranial nerves, and here even hemorrhages might be found, the extravasated red cells lying in the spaces between the connective tissue fibers (Fig. 6).

TOPOGRAPHIC STUDY

Cord: Level of the First Cervical Segment:

No lesions were seen in any of the structures in this region.

Medulla: Level of the Nuclei Gracilis and Cuneatus:

The nucleus gracilis and nucleus cuneatus showed fairly well preserved ganglion cells. The nucleus alae cinereae, however, showed a marked decrease in the number of its ganglion cells, and those remaining were

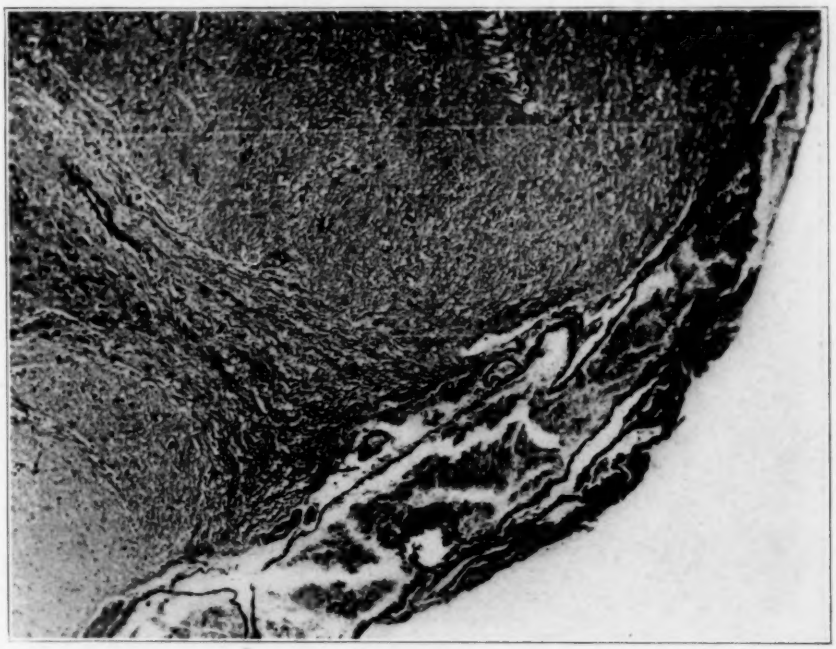

Fig. 6.—Point of exit of the nervus glossopharyngeus, showing a dilated vein and hemorrhage.

either shrunken and heavily stained or showed the reverse chromolytic change. There was marked proliferation of the glia which formed a heavy network of coarse fibrils in which were many cells of the astrocyte type (Fig. 4). There was also a considerable number of amylaceous bodies. The nucleus ambiguus showed moderate lesions of the chronic type in its ganglion cells. The nucleus nervus hypoglossi was entirely normal, its cells well preserved. The ganglion cells of the nucleus olivaris inferior were shrunken and vacuolated and the latter filled with yellow pigment.

The blood vessels throughout the section showed a slight adventitial infiltration with round cells. One perivascular hemorrhage was found.

The root fibers of the nervus hypoglossus were normal. The pia showed no lesions.

Medulla: Level of the Exit of the Nervus Glossopharyngeus:

The nucleus ambiguus, nuclei arcuati, nucleus of the nervus glossopharyngei, nuclei of the nervus cochlearis ventralis and dorsalis all showed lesions of their ganglion cells of the "chronic type," such as shrinkage, poor staining of their tigroid bodies and eccentricity of the nucleus. The nerve roots of the N. glossopharyngeus showed a definite increase in the glia nuclei throughout their medullary course, and a considerable number of amylaceous bodies. In the extramedullary portion of the root of the nervus acusticus was a large perivascular hemorrhage (Fig. 7).

Pons: Level of Exit of Nervus Trigeminus:

At this level the following nuclei showed moderate lesions of their ganglion cells consisting of shrinkage and chromolytic changes. The nuclei motorii of the nervus trigemini, nucleus nervus vestibularis superior

Fig. 7.—Perivascular hemorrhage into the root of the nervus acusticus.

and the nuclei reticularis tegmenti. No definite lesions were found in the root fibers of the nervus trigeminus. Practically all the small vessels at this level showed more or less adventitial infiltration with round cells, but there were only occasional hemorrhages.

Pons: Level of the Colliculus Superior:

The nucleus of the nervus trochlearis showed a peculiar mixture of normal ganglion cells and others with moderate lesions of the type described in the foregoing. Many of the small vessels showed a typical perivascular infiltration with round cells. Hemorrhages were much more frequent than in any of the previous sections.

Pedunculi Cerebri: Level of the Nucleus N. Oculomotorius:

The ganglion cells of the nucleus of the nervus oculomotorius were entirely normal. The cells of the substantia nigra were also normal, both in regard to their tigroid bodies and pigment. The cells in the nucleus

ruber also showed no definite lesions. At the point of exit of the root fibers of the nervus oculomotorius were several large vessels around which there were round cell infiltration and perivascular hemorrhage.

Thalamus: Level of Corpora Mammillaria:

The ganglion cells in the corpora mammillaria showed moderate chronic lesions, and there was definite neuronophagia. In the thalamus the lesions were more marked. In the nucleus anterior, medialis and lateralis thalami the ganglion cells showed the most extreme lesions, consisting of shrinkage, pallor and vacuolization (Plate 1, Fig. 4). It was in this region also that the most marked lesions were found with the Bielschowsky method (Plate 1, Fig. 3). Similar lesions were found in the upper region of the substantia nigra.

The small vessels of the thalamus showed heavy perivascular infiltration (Fig. 1) and many perivascular hemorrhages (Fig. 2). There were also areas of glial proliferation in which selective stains showed many astrocytes and coarse fibers (Fig. 3). Amylaceous bodies were also found in large numbers (Fig. 5).

These lesions were limited almost entirely to the thalamus, the subthalamic region and the tuber cinereum. The glia and vessels in the capsula interna, tractus opticus, and columna fornicis were entirely normal.

Nucleus Lentiformis:

The ganglion cells of the putamen and globus pallidus showed slight lesions of similar type to those described in the thalamus. Many, however, were normal. The small vessels also showed little if any perivascular infiltration, and no hemorrhages were found.

Nucleus Caudatus, Caput:

No definite lesions were found in the ganglion cells, the vessels or the glia of this structure. The ependyma of the ventricle was also normal.

Nucleus Amygdalae:

No lesions were noted in any of its structures.

Cerebellum:

No lesions were found in sections of various parts of the cerebellum. The ganglion cells of the nucleus dentatus and Purkinje cells stained normally.

Cerebral Cortex: Gyrus Centralis Anterior and Posterior:

Sections of the cortex in these regions showed no lesions in any of their constituents. The ganglion cells were of normal appearance when stained with both methylene blue and Bielschowsky's method (Plate 1, Figs. 1 and 2). The vessels, glia and pia also showed no lesions.

DISCUSSION

From both the clinical and anatomic findings it is evident that the case discussed is one of epidemic encephalitis extending over a period of fourteen months. From both standpoints we see evidence not of a healed process with disturbance of function from destroyed structures, but of a continuous progressive process. This is most definitely shown from the anatomic studies. In the same region are found areas of gliosis with amylaceous bodies where the process is quiescent and other areas in which the evidence of most acute inflammation is present, namely, hemorrhages.

That the virus of epidemic encephalitis may continue to live for some time is shown by the experimental transmission of the disease to rabbits in a case of six months standing by Harvier and Levaditi.[1] Economo [2] has also observed a case in which the disease extended over two years and which was studied anatomically after death. Economo describes, besides the usual acute type of lesions, areas of gliosis, some of which were spongelike in appearance, small clusters of cells, which he suggests are remnants of focal neuronophagia, cellular proliferation of the advential tissue of the veins and blood pigment in the perivascular spaces. He therefore suggests the term encephalitis lethargica subacuta for this type of the disease. Strauss and Globus [3] have also recently reported a case of subacute type of this disease, with a necropsy study, which ran a protracted course and presented symptoms of improvement, but the patient ultimately developed bulbar symptoms followed by death. Anatomically, reparative lesions were demonstrated on which were superimposed lesions of an acute type.

Our case is identical in its essentials with the one described by Economo. The distribution of the lesions is somewhat different, as in his case there were areas of gliosis in the cerebral cortex and a resulting secondary degeneration of the pyramidal tracts. The type of lesions is, however, the same, even to the peculiar areas of spongelike gliosis. Our case also shows all the lesions which have been described for the more acute type of the disease, including extensive involvement of the cranial nerve roots, as in the reports of Hammes and McKinley [4] and of Burrows.[5]

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THE SUGAR CONTENT OF THE BLOOD AND SPINAL FLUID IN EPIDEMIC ENCEPHALITIS *

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A number of investigations of the sugar content of the spinal fluid in epidemic encephalitis have been made, though few comparisons of the sugar content of the blood and spinal fluid have been published. Our investigation includes sugar determinations in both blood and spinal fluid.

LITERATURE

Marie and Mestrezat [1] report one case of epidemic encephalitis with 0.094 per cent. sugar in the spinal fluid and give as their normal figure 0.055 per cent. They do not state the method used.

Netter, Block and Dekeuwer [2] investigated fifteen cases. Their figures varied from 0.042 per cent. (fluid obtained an hour before death) to 0.097 per cent. with an average of 0.070 per cent., which is said to be above normal. In three cases the percentage of blood sugar was 0.15, 0.14 and 0.138, that for the spinal fluid from the same cases being, respectively, 0.07, 0.097 and 0.095. Their method is not given. They mention that spinal fluid sugar is slightly increased in meningism, especially in pneumonia, reporting 0.08, 0.099 and 0.063 per cent. They say that the hyperglycorrhachia is not associated with hyperglycemia, much less with glycosuria.

Dopter [3] reported one case of epidemic encephalitis with 0.085 per cent. sugar in the spinal fluid, and thought this above normal. He concludes that the hyperglycorrhachia is due to hyperglycemia.

Foster,[4] using the latest modification of the Folin-Wu method, investigated the spinal fluid in eleven cases and the blood in six of these. The spinal fluid sugar varied from 0.113 to 0.0535 per cent., an average 0.076 per cent. The blood sugar varied from 0.07 to 0.10 per cent., well within the accepted normal limits by the method used. The sugar content of twenty-two normal spinal fluids varied from

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* From the Laboratories of Columbia Hospital, Milwaukee.

1. Marie and Mestrezat: Bul. de l'Acad de méd., Paris **83**:103, 1920.

2. Netter, Block and Dekeuwer: Compt. rend. Soc. de biol. **83**:338-339, 1920; abstr. J. Nerv. & Ment. Dis. **53**:56, 1921.

3. Dopter, C.: Bull de l'Acad. de mèd. **83**:203, 1920.

4. Foster, H. E.: Hyperglycorachia in Epidemic Encephalitis, J. A. M. A. **76**:1300 (May 7), 1921.

0.0442 to 0.0614 per cent., with an average of 0.0528 per cent. Of the spinal fluids from patients with encephalitis only one, 0.0535 per cent., comes within the range of the normal.

Kraus and Pardee [5] report twelve cases in which the spinal fluid sugar varied from 0.062 to 0.095 per cent. In their tests made at Bellevue Hospital, the latest modification of the Folin-Wu blood sugar method was employed. The normal figures are given as from 0.08 to 0.12 per cent. for blood, and 0.04 to 0.06 per cent. for spinal fluid. Most of the figures for blood in the twelve cases are below 0.12 per cent. and only two are above it, 0.143 and 0.17 per cent.

Stevenson,[6] using Shaffer's method,[7] reports the sugar content of the spinal fluid in five cases as from 0.043 to 0.069 per cent., an average of 0.06 per cent. One case by the Benedecit [8] method gave 0.054 per cent. (0.043 per cent. by Shaffer's method). He quotes seven results by the Folin-Wu method (probably also included in the investigation of Kraus and Pardee) which averaged 0.0793 per cent. Stevenson calls attention to the difference between the figures obtained with the Shaffer and Folin-Wu methods. He suggests that interfering substances may cause the Folin method to give higher results. Comparisons between the two methods in a series of spinal fluids from sixteen cases of various neurologic conditions, with one exception, gave readings averaging 0.021 per cent. glucose higher by Benedict's than by Shaffer's method.

There is no standard method for determining the absolute amount of glucose in body fluids. Because different methods give different results it is impossible to arrive at a conclusion as to the absolute normal amount of sugar in spinal fluid. Each laboratory must therefore determine its own normals, and the method used must always be indicated.

Schloss and Schroeder,[9] using practically the original technic of Lewis and Benedict, concluded that "In infants and children free from meningeal disease the sugar of the cerebrospinal fluid ranges from 0.05 to 0.134 per cent. (dextrose), approximately the same range as for blood." The fluids examined were obtained from patients convalescing from disease, and so cannot be considered as normal. They also made simultaneous determinations on the blood and cerebrospinal fluid in ten cases. In only two were the values similar. They conclude that

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5. Kraus, W. M., and Pardee, J. H.: The Serology of the Spinal Fluid and Blood in Epidemic Encephalitis, Arch. Neurol. & Psychiat. **5**:710 (June), 1921.

6. Stevenson, L. D.: A Comparative Study of the Sugar Content of the Spinal Fluid in Diseases of the Nervous System, Arch. Neurol. & Psychiat. **6**:292, 1921.

7. Shaffer, P. A., and Hartmann, A. F.: J. Biol. Chem. **45**:109, 1921.

8. Benedict, S. R.: J. Biol. Chem. **34**:203, 1918.

9. Schloss, O. M., and Schroeder, L. S.: Am. J. Dis. Child. **11**:1 (Jan.), 1916.

"although the variations in the blood sugar and spinal fluid sugar are practically identical, yet there is no correspondence in the individual case at a given time." It is questionable whether the method they used or those now in use yield figures for sugar alone or for sugar and other reducing substances. The same doubt also exists regarding blood sugar. We believe that the former are neither more nor less reliable than the latter.

Leopold and Bernard,[10] using the Myers-Bailey modification of the Lewis-Benedict method, found the sugar in spinal fluid from ten normal children to vary from 0.07 to 0.107 per cent., the average being 0.074 per cent.

METHODS, MATERIAL AND DISCUSSION

The methods used in this investigation are described in detail in a preceding communication.[11] The results are given in the table of this article. Attention must be called to several details. Most specimens of blood and spinal fluid were obtained before breakfast after a fast of from twelve to fourteen hours. The blood sugar determinations were made by Benedict's and by Myers-Bailey's [12] modifications of the Lewis-Benedict [13] method. Two technics were used in examining spinal fluid by the Benedict modification of the blood sugar method. One was the original, and the other (indicated in the table as "changed") was a modification suggested by Benedict, in which the spinal fluid was diluted with five instead of two volumes of water and six and a half instead of nine and a half volumes of picrate were added in order to reduce the amount of picric acid radical in the filtrate. The protein content of spinal fluid is much less than that of blood. Hence little picrate is removed by precipitation of the protein and, if the original technic is followed, the filtrate will contain more picrate and give a deeper color than the glucose standard. We have specified in the tables the technic used as either "original" or "changed." The Myers-Bailey modification of the Lewis-Benedict method and the latest modification of that of Folin-Wu [14] were also used for the determination of sugar in spinal fluid. In the Folin-Wu method it was not found necessary to use a standard of one half the original strength, as suggested by Foster.

The methods of Myers-Bailey, Folin-Wu, and the "changed" technic of Benedict's modification give figures which are approximately the same. The original Benedict modification yields results from 10.3 to 18.5 per cent. (an average of 13 per cent.) higher than the other methods.

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10. Leopold, J. S., and Bernhard, A.: Am. J. Dis. Child. **13**:34 (Jan.), 1917.
11. Thalhimer, W., and Updegraff, H.: A Comparison of Several Clinical Quantitative Blood Sugar Methods, J. A. M. A. **78**:1383 (May 6) 1922.
12. Myers, V. C., and Bailey, C. V.: J. Biol. Chem. **24**:147, 1916.
13. Lewis, R. C., and Benedict, S. R.: J. Biol. Chem. **20**:61, 1915.
14. Folin, O., and Wu, H.: J. Biol. Chem. **41**:367, 1920.

Tables for blood sugar in normal persons given in a previous communication will be used in interpreting the blood sugar figures in the table of this article. With Benedict's modification in normal blood, taken before breakfast, the amount varied from 0.098 to 0.171 per cent. The usually accepted normal limits are from 0.08 to 0.12 per cent.

The results in three cases of general paresis were included for comparison, since, in this condition, the lesions of the blood vessels in the frontal lobes are comparable to the lesions of epidemic encephalitis in the midbrain region.

A short description of the cases of epidemic encephalitis follows:

1. Severe, lethargic type with a duration of about ten days. The patient died twelve hours after the last spinal fluid examination. Necropsy revealed characteristic lesions of epidemic encephalitis.

2. Moderately severe, lethargic and myoclonic type with gradual recovery

3. Lethargic type, not quite so severe as in Case 2.

4. A girl, aged 17 years, had the lethargic type of encephalitis. The illness progressed during a month and she died in the ambulance on the way to the hospital. Lumbar puncture was performed two hours after death. Necropsy revealed characteristic lesions of epidemic encephalitis.

5. A one and a half year old boy had encephalitis. The disease ran a peculiar course, sometimes with myoclonic twitchings, sometimes with lethargy. Lobular pneumonia and bilateral otitis media also developed. No necropsy examination was made.

6. Mild case with diplopia; recovery.

7. Mild case without lethargy but with marked excitement, sleeplessness and transitory diplopia. The illness lasted about six weeks with gradual recovery.

8. Rapidly fatal, lethargic type of one week's duration. Lumbar puncture was made ten hours before death. Necropsy examination was not allowed.

9. Mild, lethargic type of encephalitis with gradual recovery.

10. Mild case, the main symptom being diplopia; gradual recovery.

11. Mild, lethargic type, with diplopia; gradual recovery.

12. Lethargic type with periods of marked improvement and relapses during eighteen months. For three months before death parkinsonian mask, lethargy and catatonia were present. It was difficult to give nourishment, and there was extreme emaciation. Necropsy examination revealed characteristic lesions of epidemic encephalitis with unusually wide distribution.

13. Moderately severe. Spinal fluid was obtained during convalescence when the patient was almost well.

14. Fulminating case of lethargic type. Death occurred four days after the onset of the disease. Spinal fluid was obtained five hours before death. Necropsy examination was not made.

It is probably safe to assume that the upper limit of normal spinal fluid sugar with the latest modification of Folin-Wu and the method of Myers-Bailey is between 0.06 and 0.065 per cent. With the two Benedict modifications of the Lewis-Benedict method the upper normal

limit is somewhat higher, 0.075 or even 0.08 per cent., with an occasional high normal (similar to an occasional high normal blood sugar) of 0.1 per cent. Certainly some of the figures obtained in epidemic encephalitis, such as 0.117, 0.126, 0.1347, 0.161, 0.177 per cent., etc., are above normal. All are high even if not definitely abnormal.

Similarly with the figures for blood sugar, some are definitely above normal and all are high. Most are above the average obtained by us for normal blood.

More important than the amount of sugar in blood or spinal fluid in epidemic encephalitis is the demonstraton that, whatever the significance of the sugar may be, there is a quantitative relationship between the sugar content of blood and spinal fluid. When blood sugar increases spinal fluid sugar increases also. In fact, it is difficult to understand how the sugar of the spinal fluid can increase without an analogous increase in blood sugar. The constituents of the spinal fluid can come only from the blood.

In the presence of increased blood sugar it is evidently possible that pathologic conditions in the meninges or choroid plexus may hold back the glucose and prevent its entry into the spinal fluid. The patient in Case 25, who had tuberculous meningitis (verified at necropsy), showed a blood sugar content of 0.15 per cent., as high as that in some of the cases of epidemic encephalitis, yet the spinal fluid contained only 0.028 per cent. of sugar. There seems to be no *exact* quantitative relationship between the sugar in the blood and in the spinal fluid or normal persons. In them the spinal fluid sugar is, however, approximately 45 per cent. of that of the blood. In pathologic conditions this ratio changes. In epidemic encephalitis the ratio of sugar in the spinal fluid to that in the blood increases as the blood sugar increases. Thus, in Case 1 (blood sugar 0.297 per cent., spinal fluid sugar 0.177 per cent.), the ratio is 60 per cent. In chronic nephritis, Myers and Fine [15] give the ratio as 57 per cent. In Case 28, diabetes mellitus, the blood sugar was 0.275 per cent. and the spinal fluid sugar 0.234 per cent., the ratio being 85 per cent.

Our results seem to indicate that until the blood sugar reached about 0.19 per cent. there was no marked change in the sugar of the spinal fluid. This might signify that the meningeal choroid complex, as it is called by Flexner,[16] maintains a threshold level for the passage of sugar from the blood into the spinal fluid. This would be similar to the threshold maintained by the kidney for passage of glucose into the urine. It may be noted that the amount of sugar in normal urine is about the same as that in normal spinal fluid.

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15. Myers and Fine: Prac. Soc. Exper. Biol. & Med. **13**:126, 1916.

16. Flexner, S., Amoss, H. L.: J. Exper. Med. **25**:525, 1917; **28**:11-17, 1918; **27**:679, 1918.

RESULTS OF AUTHORS' INVESTIGATIONS OF SUGAR CONTENT OF BLOOD AND SPINAL FLUID IN EPIDEMIC ENCEPHALITIS

No.	Patient	Age	Sex	Date, 1921	Diagnosis	Time Obtained	Blood Sugar		Spinal Fluid Sugar				Spinal Fluid						Blood Wassermann
							Benedict	Myers	Benedict		Myers	Folin	Cells	Albumin‡	Globulin	Reduction with Fehling's†	Colloidal Gold Test	Wassermann	
									Original	Changed*									
1	A. G.	26	♂	2/ 3	Encephalitis	After breakfast	.....	.....	0.161	.....	.....	.....	175	1 mm.	Negative	Increased	Negative		
				2/ 5	Encephalitis	Before breakfast	0.297	.....	0.177										
2	S. L.	53	♂	2/15	Encephalitis	After breakfast	0.182	.....	0.126	.....	.....	.....	8	4 mm.	Negative	Normal	.....	.....	Negative
				2/17	Encephalitis	Before breakfast	0.196	.....	0.134	.....	.....	.....	...	.....	.....	.....	Negative		
				2/25	Encephalitis	Before breakfast	0.208	.....	0.117	.....	.....	.....	...	.....	.....	.....	113331000		
				3/24	Encephalitis	Before breakfast	0.150	.....	.....	0.071									
3	G. I.	42	♂	2/ 8	Encephalitis	Before breakfast	0.174	.....	0.089	.....	.....	.....	37	2 mm.	Negative	Slight reduction	Negative	Negative	Negative
				2/25	Encephalitis	Before breakfast	0.144	.....	0.082	.....	.....	.....	...	.....	.....	.....	1123331000		
4	L. F.	16	♀	3/ 2	Encephalitis	2 hrs. post-mortem	.....	.....	0.079	.....	.....	.....	150	2 mm.	Faintly positive	Increased			
5	S. E.	8 mo.	♂	3/ 7	Encephalitis	4 hrs. after breakfast	0.188	.....	.....	0.090	.....	.....	17						
6	S. M.	35	♀	2/ 6	Encephalitis	Before breakfast	0.159	.....	0.080										
7	M. M.	33	♀	2/16	Encephalitis	Before breakfast	0.155	.....	0.093	.....	.....	.....	40	4 mm.	Negative	Slight excess	Negative	Negative	Negative
				3/ 3	Encephalitis	Before breakfast	0.163	.....	0.084										
8	S. C.	20	♂	2/20	Encephalitis	10 hrs. ante-mortem	0.226	.....	0.125	.....	.....	.....	28	2 mm.	Trace	Marked reduction			
9	S. M.	32	♀	3/12	Encephalitis	3 hrs. after lunch	0.211	.....	.....	0.080			...	.....	.....	.....	.....	Negative	Negative
10	W. A.	33	♀	2/25	Encephalitis	Before breakfast	0.148	.....	0.084	.....	.....	.....	13	2 mm.	Negative	Increased	Negative	Negative	Negative

11	N. J.	20	♀	3/10	Encephalitis	Before breakfast	0.173											
				3/12	Encephalitis	Before breakfast	0.179	.....	.....	0.0854	.....	.....	96	8 mm.	Strongly positive	Increased		
				3/22	Encephalitis	Before breakfast	0.130											
12	M. M.	30	♂	7/27	Encephalitis	Before breakfast	0.115	0.104	.....	0.056	0.060	.....	1	2 mm.	Faint trace	No reduction	.....	Negative	Negative
13	S. D.	60	♂	9/21	Encephalitis (convalescent)	4 hrs. after lunch	.....	.....	.....	0.082	.....	.....	0	2 mm.	Negative	Normal	Negative	Negative	Negative
14	V. E.	45	♂	8/23	Encephalitis	5 hrs. antemortem	.....	.....	0.150	0.136	0.136	0.136	50	3 mm.	Strongly positive	Greatly increased			
15	K. J.	50	♂	3/17	General paresis	Before breakfast	0.146	.....	.....	0.062	.....	.....	13	2 mm.	Positive	Increased	5555555410	++++	++++
16	B. F.	40	♂	3/17	General paresis	Before breakfast	0.144	.....	.....	0.059	.....	.....	...	.....	.....	.....	5555555310	++++	++ +
17	F. L.	50	♂	3/17	General paresis	Before breakfast	0.146	.....	.....	0.048	.....	.....	...	.....	.....	.....	5555553100	++++	++++
18	U. G.	55	♂	3/22	Normal	Before breakfast	0.135	.....	.....	0.055	.....	0.080							
19	H. L.	55	♂	3/21	Normal	Before breakfast	0.158	.....	.....	0.074									
20	G. J.	42	♂	3/22	Normal	Before breakfast	0.129	.....	.....	0.063									
21	B. N.	30	♂	8/24	Normal	Before breakfast	.....	.....	0.064	0.054	0.058	Lost							
22	G. F.	35	♂	8/11	Normal	Before breakfast	0.115	0.094	0.053	.....	0.053	0.058							
23	K. E.	45	♂	8/11	Normal	Before breakfast	0.117	0.100	0.056	.....	0.056	0.058							
24	W. M.	50	♂	6/ 6	Brain tumor	Before breakfast	.....	.....	.....	0.179	.....	.....	...	.....	.....	.....	.....	Negative	Negative
25	T. G.	8	♂	3/18	Tuberculous meningitis	Before breakfast	0.150	.....	.....	0.028	.....	.....	180	5 mm.	Positive	No reduction			
26	M. C.	48	♂	3/12	Brain tumor	Before breakfast	0.158	.....	.....	0.079	.....	.....	10						
27	G. M.	31	♂	8/24	Diabetes mellitus	Before breakfast	.....	.....	0.158	0.143	0.150	0.143							
28	S. G.	55	♂	3/ 8	Diabetes mellitus	Before breakfast	0.275	.....	0.234										

* The technic indicated by "changed" is described in the text.

† It is of interest that the amount of reduction with Fehling's solution did not always agree with the more exact methods of quantitative determination of glucose. Fehling's test was always performed as follows: 1 c.c. Fehling's No. 1 and 1 c.c. Fehling's No. 2 mixed and diluted to 25 c.c. with distilled water. Three cubic centimeters of this dilution are boiled and 2 c.c. spinal fluid added; the solution is then boiled again.

‡ The nitric acid ring test for albumin was used, and the results recorded are the width of the white ring in millimeters.

Benedict, Osterberg and Neuwirth,[17] found that sugar in normal urine varies from 0.05 to 0.1 per cent. They used a method very similar to the Benedict method for sugar in the blood. Because of this similarity it is permissible to compare figures obtained by the Benedict method in normal spinal fluids with those obtained by the method of Benedict and Osterberg in normal urine. This comparison shows practical identity.

Shaffer found lower figures for sugar in normal urine by his method than by that of Benedict and Osterberg. Stevenson found lower figures for sugar in spinal fluid by Shaffer's than by Benedict's method. Neither Stevenson nor other investigators, so far as we have found, have reported results with Shaffer's method in normal spinal fluid.

Just as nephritic kidneys to a certain extent hold back sugar from entering the urine, so perhaps tuberculous meningitis holds back sugar from the spinal fluid. This might also explain the low sugar content of the spinal fluid in cases of acute meningococcus, or other types of purulent, meningitis, better than the breaking down of glucose by organisms present in the spinal canal.

There are three possible explanations of the hyperglycorrhachia suggested by the authors of the first three papers quoted in the review of the literature:

1. The lesions of epidemic encephalitis, situated in the midbrain and about the fourth ventricle, may act like the piqûre of Claude Bernard. The piqûre causes only temporary hyperglycemia and hyperglycorrhachia. The persistence of the lesions in epidemic encephalitis may account for the continued hyperglycorrhachia and increased blood sugar. The fact that in *early* cases of poliomyelitis the spinal fluid sugar remains low (Leopold and Bernard) is a point in favor of this view, since the lesions in this disease are similar to those in epidemic encephalitis although mainly confined to the spinal cord. It would be of interest to know whether the sugar of the spinal fluid is increased in later stages of poliomyelitis with bulbar involvement.

2. Kraus and Pardee suggest that the vascular lesions in epidemic encephalitis may render the walls of the blood vessels more permeable, so that glucose passes more readily from the blood to the spinal fluid. This theory is ingenious but is not necessary to explain the facts since the blood sugar is increased in this disease and the increase of sugar in the spinal fluid is probably secondary to that in the blood.

3. The increase in the sugar of both the blood and spinal fluid may be caused by a general reaction to the infectious agent of epidemic encephalitis. Hirsch[18] has recently shown in animals that the intra-

17. Benedict, Osterberg and Neuwirth: J. Biol. Chem. **34**:217, 1918.
18. Hirsch, Edwin F.: J. Infect. Dis. **29**:40, 1921.

venous injection of bacteria causes a rise in blood sugar. It is also known that many infectious diseases are associated with hyperglycemia.

CONCLUSIONS

1. The sugar content of the blood and spinal fluid is increased in epidemic encephalitis.

2. The sugar of the spinal fluid appears to increase only after a certain level of blood sugar has been reached. This might be considered a threshold level for sugar in the spinal fluid such as the kidneys maintain for sugar in the urine.

3. The hyperglycorrhachia and hyperglycemia may be due to the cerebral lesions of epidemic encephalitis or to the general infection.

4. There must be a considerable extension of our knowledge of the amount of sugar in normal and pathologic spinal fluid before the diagnostic significance of hyperglycorrhachia can be established.

5. At present hyperglycorrhachia can be used chiefly to differentiate epidemic encephalitis from the two conditions with which it is most likely to be confused—tuberculous meningitis and early poliomyelitis.

XANTHOCHROMIA DUE TO ACUTE, PURULENT SPINAL MENINGITIS

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Since Froin's [1] classical studies on xanthochromia in 1903, much has been added to our knowledge of yellow spinal fluid, both as to its chemical and cytologic contents, and the varied conditions under which it may be encountered. Sprunt and Walker,[2] in 1917, analyzed 100 reported cases and added five personal reports. From their conclusions it would seem wise to divide xanthochromatic spinal fluids into two classes which, given in their own words, are as follows:

1. Those in which the color is due to dissolved hemoglobin or its derivatives, and which, as a rule, do not coagulate spontaneously and contain only a small amount of globulin. Such fluids usually are associated with brain tumor in contact with the meninges or the ventricles.

2. The larger and more important group comprises those cases showing the so-called Froin's syndrome, in which the fluid is transparently clear, yellow, coagulates spontaneously, contains large amounts of globulin, may or may not show pleocytosis, and gives no positive tests for hemoglobin. This is a "compression syndrome," its main determinants being the isolation of a lumbar cul-de-sac, in which the spinal fluid stagnates, and probably some vascular changes within its walls.

It is the latter type of xanthochromia that is so likely to be associated with spinal cord tumor, although many other conditions involving the cord have been reported in which the syndrome has occurred. When an actual pocket of the subarachnoid space is not isolated, the syndrome usually differs in some respects from that described originally by Froin, most often perhaps in the absence of spontaneous, "massive coagulation."

Elsberg and Rochfort [3] in a study of ninety-two cases of chronic diseases of the spinal cord found xanthochromatic cerebrospinal fluid in fourteen instances. Of these, twelve were either spinal cord tumor or gumma; one was an example of varicose veins of the cord and one a case of neuritis of the cauda equina. In seven of the cases Froin's syndrome of massive coagulation was present, all being examples of tumor of the conus or cauda equina. The so-called syndrome of Nonne,[4]

1. Froin: Gaz. d. hôp., Sept. 3, 1903.
2. Sprunt and Walker: Bull. Johns Hopkins Hosp. **28**:80-86, 1917.
3. Elsberg, C. A., and Rochfort, E. L.: Xanthochromia and Other Changes in the Cerebrospinal Fluid, J. A. M. A. **68**:1802, 1917.
4. Nonne: Deutsch. Ztschr. f. Nervenh. **47**:436, 1913.

that is, excess of globulin without cell increase, these authors found more frequently in tumors at a higher level.

I herewith report a case not showing coagulation and not due to tumor, although the excessive and heaped-up exudate seemed almost necessarily to have isolated a lumbar cul-de-sac.

REPORT OF A CASE

History.—H. W. J., a white man, aged 61, was seen in consultation with Dr. Rockwell of Cambridge, Mass. The clinical diagnosis of the case was meningitis; xanthochromia. Necropsy revealed a massive, exudative spinal meningitis.

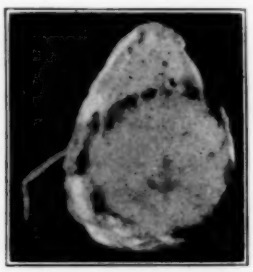
His family and past history were negative. For three weeks before consultation, the patient had had a mild catarrhal rhinitis, with a temperature irregularly elevated, but never above 100 F. He continued going to business until March 18, 1921. On the evening of this date he had a temperature of 101 F. and a pulse rate of 100. The general physical examination was negative. The next morning his temperature was 104, his pulse rate 120, and he suffered from moderate backache, restlessness and anorexia. The same evening his temperature had fallen to 101, but there were periods of Cheyne-Stokes respiration, and the patient perspired freely. Later in the evening he became first semiconscious and finally completely unconscious. The next morning, March 20, he was conscious again; pain in the back continued, and there was a slight unproductive cough. Examination of the lungs revealed a small area in the left upper lobe which was dull, and tubular breathing. The urine examination was negative except for a trace of albumin and an occasional cast.

During the next three days the patient seemed to improve subjectively, was conscious and quite cheerful, though the temperature ranged between 100 and 102 F. During the night of March 23, however, he again became semiconscious, respirations were rapid, and his temperature went up to 103.5. On March 24, I saw him for the first time.

Physical Examination.—The patient was lying in bed with a cold compress on his forehead. He was conscious and answered questions rationally, but there was a tendency to muttering, and his speech was confused at times. Involuntary urination was observed. Temperature by mouth was 104 F. and perspiration was profuse. Respirations were rapid but regular. There was definite, though not marked stiffness of the neck, and Kernig's sign was positive. Knee and ankle reflexes were present and equal on both sides. No ankle clonus was present. The Babinski sign was positive on both sides. The optic disk outlines were distinct with moderate venous congestion but no elevation of the disks.

Lumbar Puncture.—Ten cubic centimeters of canary yellow, slightly turbid fluid were removed. There was no increase in pressure, the fluid coming out in ordinary, rapid drops. There were 250 polymorphonuclear leukocytes per cubic millimeter. The albumin reaction was + + +. There was no sugar. Cultures of the fluid on blood-serum agar showed no growth in two days, and no organisms were seen by smear. The fluid was anticomplimentary to the Wassermann reaction, and it did not clot even after the addition of a drop of blood. The patient's condition continued to become worse, and he died at 6 a. m., March 25. A necropsy confined to the spinal cord was performed on the afternoon of the same day.

Gross Pathology of the Spinal Cord.—The cord was removed from the second cervical segment to the end of the cauda equina. There was considerable yellow, thick, fibrinopurulent exudate extending from about the third cervical segment to between the third and fourth lumbar segment, lying mainly over the posterior and lateral surfaces of the cord and continuing below the third lumbar segment to the posterior surface of the cauda equina for a distance of about 4 cm., but not extending laterally or beyond the lateral surfaces of the nerves making up the cauda. On lifting the cord out, it was noted anteriorly that this exudate, although occupying mainly the regions mentioned, extended around to the ventral surface of the cord over nearly its entire extent, but here it was much thinner and inconspicuous. The principal thing to be noticed in regard to the configuration of the exudate was that beginning at about the eighth dorsal segment and extending downward a distance of 6 cm. on the posterior surface, that is, to the eleventh dorsal segment, the exudate formed a considerable ridge of triangular shape on cross section, its base being on the posterior surface of the cord and the apex of the ridge in its highest point standing 6 mm. above the surface.



Section of cord showing exudate at level of tenth dorsal segment; ×2.

Section from Level of Eleventh Dorsal Segment.—The section showed a thick, enveloping meningeal exudate of polymorphonuclear leukocytes, lymphoid cells and much fibrin. On the posterior surface, this exudate was caked into a layer, somewhat cone-shaped, and about 6 mm. in thickness. Within the meshes of the fibrin there were in places, numerous isolated, round dots, about the size of the ordinary pyogenic cocci. There were no chains or clumps of these elements, and they were entirely extracellular.

COMMENT

Whether the exudate by compression and adhesion actually isolated a portion of the lumbar subarachnoid space, could not be ascertained at the time of the necropsy. This seems probable, however, from the unusual finding of yellow spinal fluid. A substantiating fact, from the bacteriologic side, was the failure of any organisms to grow on blood-serum agar from cultures of the fluid withdrawn at lumbar puncture, the fluid thus obtained coming of course from the presumably isolated lumbar cul-de-sac.

A SUGGESTION FOR THE USE OF DYES IN THE LOCALIZATION OF SPINAL CORD TUMORS AT OPERATION

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The recent work of Ayer[1] on the use of combined cistern and lumbar puncture for the detection of spinal subarachnoid block, and the work of Dandy and Blackfan[2] on the use of dyes in the diagnosis of obstructive hydrocephalus, have suggested a procedure which may be of use in the localization of spinal cord tumors at operation.

In principle the method consists of two steps: first, the demonstration of spinal subarachnoid block, by the Ayer method; second, the injection of a dye into the cisterna magna, or into the lumbar subarachnoid space. The injection is made immediately prior to operation. Assuming that the lumbar route has been used, the dye will diffuse through the subarachnoid space up to the lower pole of the tumor. The existence of a subarachnoid block will prevent its going beyond this point. If the laminectomy opening is below the tumor, on opening the dura a deep blue stained fluid will be encountered. The laminectomy must then be extended upward. If, on the other hand, the laminectomy has been above the level of the tumor, on opening the dura a colorless fluid will be encountered. The opening must then be continued downward.

The two cases here reported in brief have given an opportunity of testing the method.

REPORT OF CASES

CASE 1.—*History.*—W. H. G., a man, aged 54, single, seen Nov. 3, 1921, three years ago had pains in the right axilla, gradually increasing in intensity and aggravated by coughing and sneezing. Seven months ago there was numbness of the feet, gradually ascending over the legs and trunk to the level of the second interspace in front. Weakness and stiffness of the legs increased. Bladder weakness was present. For several months he had been bedfast owing to weakness and rigidity of the legs.

Physical Examination.—This revealed: Arms and hands normal; abdominal and cremasteric reflexes absent; marked weakness of the legs, extreme spasticity, exaggerated reflexes, bilateral ankle clonus and Babinski sign. Sensa-

1. Ayer, J. B.: Spinal Subarachnoid Block as Determined by Combined Cistern and Lumbar Puncture, Arch. Neurol. & Psychiat. **7**:38 (Jan.) 1922.

2. Dandy and Blackfan: Internal Hydrocephalus, Am. J. Dis. Child. **8**:406 (Dec.) 1914.

tion: Anesthesia to touch reached the second interspace in front and the fourth dorsal spine behind. It extended a short distance down the inner aspect of the arm.

Diagnosis.—Cord tumor; extramedullary; level of second dorsal segment.

Combined Cistern and Lumbar Puncture.—Puncture revealed:

	Cistern	Lumbar
Pulsation of fluid with pulse and respiration	Very active	Present but less active
Initial pressure	75 mm. water	15 mm. water
After removal of 4 c.c. from lumbar spine	65 mm. water	0 mm. water
After removal of 7 c.c. from cistern	15 mm. water	0 mm. water
Appearance of fluid	Slightly turbid	Yellow
Globulin	++	++++
Cell count	0	1

The findings on combined puncture indicated complete spinal subarachnoid block.

Operation.—Nov. 15, 1921, operation was performed by Dr. T. M. Joyce. Immediately before the operation, with the patient under the anesthetic, 1 c.c. of a concentrated indigo-carmin solution was injected into the cisterna magna. Laminectomy followed at once, including the sixth cervical to the second dorsal laminae. The dura was exposed. The tumor could be palpated beneath the dura at about the middle of the laminectomy opening. A small nick was made in the dura below the tumor. The spinal fluid welling up through the nick showed a faint bluish tinge. A nick was then made in the dura above the tumor. The fluid here showed a deep blue stain. The contrast between the two was marked. It became still more marked on complete opening of the dura. Above the tumor, the arachnoid was bulged out, cystic and stained deep blue. Below the tumor only a faint blue staining of the arachnoid was evident. The tumor which was about 2.5 by 1.5 cm. in diameter was readily removed.

Pathologic Report (by Dr. R. L. Benson).—Endothelioma.

As stated in the foregoing, combined cistern and lumbar puncture in this case showed evidence of a complete spinal subarachnoid block. In spite of this, due doubtless to the relaxation of the tissues attendant on the general anesthesia, a small amount of the dye had leaked past the block, slightly staining the arachnoid and the fluid below the tumor.

CASE 2.—*History.*—J. P. F., a man, aged 48, married, seen Sept. 14, 1921, three years ago had a pain in the back, about the level of the third to the fifth lumbar spines, worse on the right. The pain radiated into the side and lower half of the abdomen. It gradually increased in intensity and was worse on coughing and sneezing. Two months ago he felt weak and stiff, first in the right leg then in the left. There was numbness of both legs. He had dysuria for two weeks.

Physical Examination.—This revealed: right upper abdominal reflex weak; left upper better; right lower absent; left lower absent; well marked positive Beevor sign. Legs: Both legs showed marked weakness and spasticity, with exaggerated knee reflexes and Achilles' reflexes, bilateral ankle clonus and a positive Babinski sign. Sensation: There was anesthesia to touch beginning on the right 2.5 cm. below the umbilicus, in front, and at the second lumbar spine behind. On the left the level of anesthesia was about 2.5 cm. lower.

Diagnosis.—Cord tumor; extramedullary; level of tenth dorsal segment.

Combined Cistern and Lumbar Puncture.—Puncture Sept. 17, 1921, revealed:

	Cistern	Lumbar
Initial pressure	150 mm. water	170 mm. water
Appearance	Clear, colorless	Clear, colorless
Globulin	+	++++
Cell count	2	4
November, 1921:		
Pulsation	Very active	Slight
Initial pressure	180 mm. water	160 mm. water
After removal of 5 c.c. from lumbar region	160 mm. water	45 mm. water
After removal of 6 c.c. from cistern	80 mm. water	40 mm. water

The findings on combined puncture again pointed to complete spinal subarachnoid block.

Operation.—Operation was performed by Dr. J. D. Sternberg. Immediately before the operation, with the patient under the anesthetic, spinal puncture was performed. Seven cubic centimeters of fluid were withdrawn and 5 c.c. of a concentrated indigo-carmin solution injected. Laminectomy included the seventh to the tenth dorsal laminae. The tumor, though quite small, was clearly visible before opening the dura. Here again it was possible to nick the dura above and below the tumor. Both fluids were clear and colorless. The dura was then incised for the full length of the laminectomy opening. The arachnoid below the tumor was distended with clear fluid, forming a small, cystlike sac. On incising the sac, a deep blue stained fluid welled up from below. During the removal of the tumor, more of this blue stained fluid flowed out from time to time. The fluid pouring down from above the tumor remained persistently clear and colorless. The tumor was about 1 by 1 cm. in diameter. It was readily removed.

Pathologic Report (by Dr. R. L. Benson).—Endothelioma.

In the two cases presented the clinical picture was clear cut, and an accurate preoperative localization of the tumor was possible. But this does not always happen. At times, only an approximate localization can be made. In such cases, the procedure suggested in the foregoing may prove of value.

COMMENT

One must first demonstrate, by the Ayer method, the existence of a spinal subarachnoid block. If no block is present, the dye will leak past the tumor and stain the arachnoid and the fluid both above and below it. Even when a complete block has been demonstrated traces of the dye may leak past the tumor, as happened in Case 1.

Qf the two routes by which the dye may be injected (cistern and lumbar) the lumbar route is preferable. It gives a greater concentration of the dye, and a lesser chance of leakage past the tumor. Five cubic centimeters of a concentrated indigo-carmin solution is sufficient to give a deep stain to the spinal fluid and the arachnoid below the tumor. The solution must, of course, be carefully sterilized.

Having localized the tumor as accurately as possible and chosen the site of operation, spinal puncture is performed; from 6 to 8 c.c. of fluid are removed, and 5 c.c. of the sterile dye solution injected. Laminectomy is then performed. The dura is opened. If one is below

(caudad to) the level of the tumor, a fluid stained deep blue will be found. The laminectomy must then be extended upward. If the opening is above (cephalad to) the tumor, clear fluid will be obtained, and the incision must be extended downward.

It is conceivable that this method may be of value also in outlining the lower margin of arachnoid cysts. These cysts may produce all the symptoms of spinal subarachnoid block and cord compression, but may be difficult to detect at operation owing to the delicacy of the cyst wall. The presence of the dye solution extending up to, but not beyond such a structure, and staining its lower margin, might be of considerable aid in determining the diagnosis at the time of operation.

STUDIES ON THE CEREBROSPINAL FLUID AND BLOOD IN MULTIPLE SCLEROSIS *

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In a disease presenting such marked pathologic changes as multiple sclerosis, one might confidently expect abnormalities, perhaps characteristic, in the cerebrospinal fluid. Yet a review of the literature fails not only to reveal findings pathognomonic of the disease, but shows that many authors regard the fluid as essentially normal. In a recent comprehensive paper [1] dealing with the differential diagnosis of multiple sclerosis the significance of fluid tests is evidently considered nil as no mention is made of them. The opinions of writers prior to 1909 are summarized by Szecsi [2]: of ninety-five case reports collected by him pleocytosis was reported in forty-five. A few years later the gold chlorid test of Lange came into use. Flesch [3] reports a "paretic" colloidal gold curve in six of eight cases; Kaplan,[4] in one of eighteen cases; Hammes,[5] one paretic curve in four cases; Eskuchen,[6] states that 50 per cent. of the fluids are entirely normal; of the 50 per cent. abnormal, increase in pressure, pleocytosis and a strong globulin reaction are found, and in 20 per cent. the paretic colloidal curve. Adams [7] reports the paretic curve in five cases and the syphilitic curve in thirty-four. Moore [8] finds the paretic reaction in eighteen of twenty cases,

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* Read at the Meeting of the Association for Research in Nervous and Mental Diseases, New York, Dec. 28-29, 1921.

1. Rotter, R.: Zur Differentialdiagnose der Multiplen Sklerose, Deutsch. Ztschr. f. Nervenh. **71**:45, 1921.

2. Szecsi, S.: Beitrag zur Differentialdiagnose der Dementia paralytica, Sclerosis multiple und Lues cerebrospinalis, Monatsch. f. Psychiat. u. Neurol., 1909, p. 352.

3. Flesch, M. E.: Die Untersuchung des Liquor cerebrospinalis mit Kolloidaler Goldlosung, Ztschr. f. d. ges. Neurol. u. Psychiat. **26**:318, 1914.

4. Kaplan, D. M.: Die characteristische Ausflockung Kolloidalen Goldes durch der Liquor progressiver Paralytiker, Ztschr. f. d. ges. Neurol. u. Psychiat. **27**:246, 1915.

5. Hammes, E. M.: The Comparative Value of the Wassermann, the Colloidal Gold and Other Spinal Fluid Tests: A Study of 203 Cases, Am. J. Med. Sc. **154**:625, 1917.

6. Eskuchen, K.: Die Lumbalpunktion, 1919, p. 146.

7. Adams, D. K.: The Cerebro-Spinal Fluid in Disseminated Sclerosis, Lancet **1**:420 (Feb. 26), 1921.

8. Moore, J. E.: The Cerebrospinal Fluid in Multiple Sclerosis, Arch. Int. Med. **25**:58 (Jan.) 1920.

with the highest cell count 70, while Warwick and Nixon [9] report only one such reaction in twenty cases, although a "strong" gold reaction was obtained in 45 per cent. of all cases. Thompson [10] reports the paretic curve in five cases of psychopathic persons with multiple sclerosis, one confirmed at necropsy.

Aside from pleocytosis in some cases, never very high; a globulin increase in some cases, seldom great; and a colloidal reaction in some cases, not infrequently in the "paretic zone," no writer claims changes which can be construed as indicative of multiple sclerosis, certainly not pathognomonic.

What are the reasons for such great variations in observations? It is not likely that laboratory errors are as great as the variations here recorded. Unquestionably errors in diagnosis must be considered as possible in this disease; but again, errors in the clinic can hardly account for such great diversity in findings, applying as they do not only to different workers, but to different cases examined by the same person. Is it possible, as Hammes and Flesch suggest, that the activity of the pathologic process determines the type of change found in the fluid?

To add to the cases on record, to attempt a correlation of clinical and laboratory findings, and to add certain chemical studies in this disease is our aim in this paper.

PERSONAL OBSERVATIONS

We were able to collect the reports of thirty-eight cases personally known to one or both of us from a clinical or laboratory aspect. Many of the patients have been followed for a number of years and all show a clinical picture which admits of little doubt as to the diagnosis. Fourteen of these were males, twenty-four females. No case was accepted in which the first symptom developed late in life, and it will be seen in the chart that the fluids examined were mostly from young adults. Furthermore, no patient presenting a positive Wassermann reaction either in the blood or fluid, was admitted.

Character of Fluid.—The fluid was invariably clear, colorless and without clot.

Pressure.—Pressure, measured in a number of the patients, was never above the limit of normal, was usually in the mid-normal zone, but frequently low. There was nothing about the pulse and respiratory oscillations to cause comment, and when jugular compression was employed the rise of pressure was prompt, indicative of the absence of meningeal or other block in the spinal subarachnoid space.

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9. Warwick, M., and Nixon C. E.: A Study of the Colloidal Gold Reaction and Its Clinical Interpretation, Arch. Int. Med. **25**:119 (Feb.), 1920.

10. Thompson, L. J.: Interpretation of the "Paretic Curve" in Lange's Colloidal Gold Test, Arch. Neurol. & Psychiat. **5**:131 (Feb.), 1921.

Cells.—Fifty-one counts in thirty-six patients may be briefly summarized thus: 0-5 cells, 29 counts; 6-10 cells, 8 counts; 11-20 cells, 8 counts; 21-30 cells, 2 counts, and 42 cells, 1 count. Differential cell studies were made only so far as possible in the cell-counting chamber, employing a faint gentian violet stain and acetic acid, and using a high objective. The cells were lymphocytes and large mononuclear cells, the latter probably arachnoid in origin.

Total Protein.—Total protein was estimated by a number of tests, but during the last two years by a quantitative method.[11] Where this latter method was employed the readings were usually found to be just below the high normal limit of 40 mg. per 100 c.c. The highest was 111 mg., the lowest 22 mg. Taking all of the tests into consideration, one half of the patients showed protein increase, never of high degree.

Globulin Tests.—Tests were made almost exclusively by the ring test with saturated ammonium sulphate (Ross-Jones modification of Nonne). Of thirty-one patients in whom this examination was made, twenty-two gave a negative and nine a positive reaction. The globulin ring was never conspicuous; it never approached the density commonly seen in general paresis.

The Wassermann Test.—This test was negative throughout in every case. One weakly positive reaction in a patient presenting on two other occasions negative reactions, one anticomplementary, and one unsatisfactory (unexplained) reaction are exceptions which do not seem to vitiate the diagnosis in these cases.

Gold Chlorid Tests.—The tests in 1914-1917 were performed under the direction of Dr. W. A. Hinton by a method described by him;[12] those of 1920 and 1921 by one of us (H. E. F.) by the following method: To 1,000 c.c. of triply distilled water in an Erlenmeyer flask are added, at 60 C., 6 c.c. of a 2 per cent. aqueous solution of potassium carbonate; immediately 10 c.c. of a 1 per cent. aqueous solution of gold chlorid (acid) are added. A Meaker burner is then substituted for the Bunsen burner and the temperature rapidly raised to 90 C., when 6 c.c. of a 1 per cent. solution of formaldehyd is added drop by drop, the flask being agitated continuously. The flask with its colorless contents is then removed from the flame and gently rotated until a bright cherry-red color, with a light golden sheen, appears, which is usually after three minutes, but before six or seven minutes. Merck's highest chemicals are used.

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11. Denis, W., and Ayer, J. B.: A Method for the Quantitative Determination of Protein in Cerebrospinal Fluid, Arch. Int. Med. **26**:436 (Oct.), 1920.

12. Lee, R. I., and Hinton, W. A.: A Critical Study of Lange's Colloidal Gold Reaction in Cerebrospinal Fluid, Am. J. Med. Sc. **148**:33, 1914.

TABLE 1.—Record of Cases

No.	Sex	Age	Date	Fluid from Puncture	Pressure, Mm.	Cells	Total Protein		Cerebrospinal Fluid										Blood								Symptoms
							Alcohol Ppt.	Mg. %	Globulin	Wassermann	Colloidal Gold Test	Sugar	Nonprotein N.	Chlorids	Acetone	Creatinin	Urea	Uric Acid	Wassermann	Sugar	Nonprotein N.	Chlorids	Acetone	Creatinin	Urea	Uric Acid	
1	F	29	1915	Lumbar	...	4	sl.+	...	...	—	0123000000	.....	....	...	...	....	....	....	—	.....	....	...	...	....	....	....	2 years, progressive
		35	1921	Lumbar	90	2	0	28	0	—	5432100000	.....	....	...	...	....	....	....	..	.....	....	...	...	....	....	....	8 years, moderately progressive
2	F	23	1920	Lumbar	100	8	+	...	+	—	5554430000	.....	....	...	...	....	....	....	—	.....	....	...	...	....	....	....	2½ years, moderately progressive
3	F	30	1921	Lumbar	...	4	sl.+	38	sl.+	—	5555542100	.....	....	...	...	....	....	....	—	.....	....	...	...	....	....	....	1 year, progressive
4	F	23	1920	Lumbar	70	6	0	38	0	Unsatisfact'y	5553210000	.....	....	...	...	....	....	....	—	.....	....	...	...	....	....	....	3 years, progressive
5	F	33	1920	Lumbar	85	7	0	50	0	—	4443211000	.....	....	...	...	....	....	....	—	.....	....	...	...	....	....	....	4½ years, progressive
6	F	26	1920	Lumbar	...	12	0	...	0	—	5553100000	.....	....	...	...	....	....	....	—	.....	....	...	...	....	....	....	5 years, progressive
7	F	31	1921	Lumbar	...	8	0	47	0	—	5555531000	.....	....	...	...	....	....	....	—	.....	....	...	...	....	....	....	2½ years, progressive
8	M	35	1920	Lumbar	50	0	0	24	0	—	5543210000	0.054	....	...	...	....	....	....	—	.....	....	...	...	....	....	....	3 years, slowly progressive
9	M	30	1920	Lumbar	70	0	+	34	0	—	5555321000	0.069	....	...	...	....	....	....	—	.....	....	...	...	....	....	....	Several years, slowly progressive
10	M	70	1921	Lumbar	...	..	sl.+	93	0	—	5554210000	.....	....	...	...	....	....	....	—	.....	....	...	...	....	....	....	30-35 years, stationary, asylum case
11	F	34	Apr., 1921	Cistern	80	2	0	22	0	—	0000000000	.....	....	...	...	....	....	....	..	.....	....	...	...	....	....	....	6 years, moderately progressive
			Apr., 1921	Lumbar	80	2	0	42	0	—	0011100000																
			Nov., 1921	Cistern	...	0	0	28	0	—	5555500000	0.065	28.5	695	0	1.25	24.3	Tr.	—	0.099	40.0	465	0	1.39	26.1	2.8	No apparent change since previous examination
			Nov., 1921	Lumbar	...	1	0	29	0	—	5555521000	0.067	18.7	686	0	1.20	17.5	Tr.									
12	M	29	4/17/20	Lumbar	60	20	+	...	+	wk.+	5555532000	.....	....	...	...	....	....	....	—	.....	....	...	...	....	....	....	Rapidly progressive, 1½ years
			5/25/20	Cistern	110	12	sl.+	100	0	—	5555542000																
			5/25/20	Lumbar	...	30	+	111	sl.+	—	5555421000																
			11/21/21	Cistern	120	19	0	22	0	—	5555421000	0.048	25.5	701	0	....	21.1	Tr.	—	0.100	....	...	...	....	....	1.9	Progressive
				Lumbar	...	18	sl.+	42	0	—	.....	0.058	17.0	693	0	....	15.9	Tr.									
13	M	42	1921	Lumbar	...	1	0	69	0	—	0115322000	0.088	....	...	...	....	....	....	—	.....	....	...	...	....	....	....	10 years, not progressive
14	F	38	1921	Lumbar	150	0	0	30	...	—	0001211000	0.067	40.7	651	...	2.38	....	....	—	.....	26.2	404	...	1.88	17.6	....	16 years, not progressive
15	F	46	1921	Lumbar	170	0	0	34	...	—	0122210000	0.080	28.1	672	...	2.30	....	....	—	.....	20.2	463	...	1.91	14.2	....	16 years, not progressive
16	F	48	1921	Lumbar	...	0	0	28	0	—	5310000000	0.061	18.2	602	...	....	....	....	—	.....	....	...	...	....	....	....	2 years, progressive
17	M	64	1921	Lumbar	...	0	0	42	0	—	0000000000	0.088	17.0	746	0	....	14.2	Tr.	—	0.080	23.9	622	0	....	15.1	2.2	About 25 years, not progressive
18	F	56	1921	Lumbar	...	4	0	57	0	—	0000000000	0.069	16.9	685	0	....	....	....	—	0.101	26.2	486	0	....	14.7	1.4	About 25 years, not progressive 3 yrs.
19	F	32	1921	Lumbar	...	4	0	50	0	—	5554310000	0.061	*	681	0	....	0	Tr.	—	.....	....	...	0	....	....	....	4 years, progressive
20	F	60	1915	Lumbar	...	2	0	50	0	—	0000000000	0.077	26.3	703	0	....	....	....	—	0.102	26.3	505	0	....	17.6	2.6	Many years, not progressive
21	M	32	1915	Lumbar	200	..	0	...	0	—	003 311000	.....	....	...	...	....	....	....	—	.....	....	...	...	....	....	....	2 years, moderately progressive
22	M	36	1915	Lumbar	120	5	+	...	+	—	0000000000	.....	....	...	...	....	....	....	—	.....	....	...	...	....	....	....	6 years, not progressive
23	M	16	1916	Lumbar	...	0	sl.+	...	0	—	0000000000	.....	....	...	...	....	....	....	—	.....	....	...	...	....	....	....	8 years, moderately progressive
24	F	18	1915	Lumbar	...	14	sl.+	...	sl.+	—	4445821000	.....	....	...	...	....	....	....	—	.....	....	...	...	....	....	....	8 months, progressive
			1917	Lumbar	65	5	+	...	+	—	.....	.....	....	...	...	....	....	....	..	.....	....	...	...	....	....	....	Not progressive
25	F	27	1916	Lumbar	...	0	0	...	...	—	0000000000	.....	....	...	...	....	....	....	—	.....	....	...	...	....	....	....	3 years, not progressive
26	F	32	1916	Lumbar	150	3	0	...	...	—	.....	.....	....	...	...	....	....	....	—	.....	....	...	...	....	....	....	11 years, not progressive
27	F	36	1921	Cistern	...	0	0	25	sl.+	..	.....	.....	....	...	...	....	....	....	—	.....	....	...	...	....	....	....	17 years, moderately progressive
				Lumbar	130	0	0	30	sl.+	—	"Paretic zone"																
28	M	35	1916	Lumbar	140	7	0	...	...	—	"Negative"	.....	....	...	...	....	....	....	—	.....	....	...	...	....	....	....	3 years, moderately progressive
			1920	Lumbar	190	4	+	...	0	—	.....	.....	....	...	...	....	....	....	—	.....	....	...	...	....	....	....	Recently progressive
			1921	Lumbar	140	6	+	44	+	—	.....	.....	....	...	...	....	....	....	..	.....	....	...	...	....	....	....	Improving
29	M	29	1912	Lumbar	180	1	0	...	...	—	.....	.....	....	...	...	....	....	....	—	.....	....	...	...	....	....	....	9 years, not progressive
30	F	43	1915	Lumbar	200	12	+	...	+	—	1232100000	.....	....	...	...	....	....	....	—	.....	....	...	...	....	....	....	1 year, progressive
31	F	30	Apr., 1919	Lumbar	...	19	+	...	+	Anticomp.	.....	.....	....	...	...	....	....	....	—	.....	....	...	...	....	....	....	4 years, paraplegia recent
			June, 1919	Lumbar	...	24	+	...	+	—																	
			July, 1919	Lumbar	...	42	+	...	0																		
32	M	26	1916	Lumbar	80	10	0	...	...	—	0015554200	.....	....	...	...	....	....	....	—	.....	....	...	...	....	....	....	9 months, progressive
33	F	35	1919	Lumbar	...	0	0	...	0	—	.....	.....	....	...	...	....	....	....	—	.....	....	...	...	....	....	....	9 years, not progressive
34	M	58	1914	Lumbar	...	8	0	...	...	—	0000000000	.....	....	...	...	....	....	....	—	.....	....	...	...	....	....	....	18 years, not progressive
35	F	37	12/13/16	Lumbar	...	3	...	...	0	—	0012322100	.....	....	...	...	....	....	....	—	0.133	....	...	...	....	....	....	Rapidly progressive paraplegia, 7 mos.
			1/3/17	Lumbar	...	..	0	..	...	..	5555553200	.....	....	...	...	....	....	....	..	.....	....	...	...	....	....	....	Laminectomy for cord tumor; necropsy: multiple sclerosis
36	F	31	1920	Lumbar	...	2	+	...	0	—	1112210000	.....	....	...	...	....	....	....	—	.....	....	...	...	....	....	....	Progressive
37	M	37	1920	Lumbar	...	3	0	...	0	—	.....	.....	....	...	...	....	....	....	—	.....	....	...	...	....	....	....	4 years, not progressive
38	F	34	1916	Lumbar	...	8	0	...	...	—	4001100000	.....	....	...	...	....	....	....	..	.....	....	...	...	....	....	....	3 years, Progressive
			1920	Lumbar	...	0	0	...	0	—	1110000000	.....	....	...	...	....	....	....	—	.....	....	...	...	....	....	....	Not progressive

* Too low to read.

Forty-two gold chlorid readings are available, obtained in thirty-three patients. The results may be summarized as follows: So-called paretic type, 21 fluids in 16 patients; so-called syphilitic type, 7 fluids in 7 patients; other positive reactions, 3 fluids in 3 patients; and negative reactions, 11 fluids in 10 patients. The paretic type was found by us in 50 per cent. of all fluids and also in nearly one half of the patients in whom this test was applied.

Sugar.—Fourteen findings are recorded. The highest is 0.088 per cent., the lowest 0.048 per cent.; the average 0.068 per cent. The method employed was that described in a recent paper,[13] a modification of the Folin-Wu technic for blood.[14]

Nonprotein Nitrogen.—Of the eleven determinations by the Folin-Wu method,[14] one was too low to read. The lowest readable was 16.9 mg. and the highest 40.7 mg. per 100 c.c. The average was 21.5.

Chlorids.—The highest of eleven determinations was 746, the lowest 51, with an average of 688 mg. per 100 c.c. The technic was that described by Whitehorne.[15]

Acetone Bodies.—No evidence of acetone bodies, B-hydroxybutyric acid, aceto-acetic acid and acetone, was found in any of the nine examinations, using the mercuric sulphate method of Van Slyke-Fitz.[16]

Creatinin.—The average of the determinations was 1.78 per 100 c.c.

Urea.—In one of the six determinations a slight trace only was found. The average was 15.5 mg. per 100 c.c.

Uric Acid.—Although a slight trace was present in all of the specimens examined, the amount was too low to read. Creatinin, urea and uric acid were tested for by the methods of Folin-Wu.[14]

OBSERVATIONS ON BLOOD

While the primary object was the study of the cerebrospinal fluid, it seemed wise to correlate the blood findings on specimens taken at the same time as the fluid. Whenever the amount of blood was sufficient, a Wassermann test was made. However, either at this time or at some other, all of the thirty-eight patients have given negative blood Wassermann reactions.

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13. Foster, H. E.: Hyperglycorachia in Epidemic Encephalitis, J. A. M. A. **76**:1300 (May 7), 1921.

14. Folin, O., and Wu, H.: A System of Blood Analyses, J. Biol. Chem. **38**:81, 1919; **45**:449, 1920.

15. Whitehorne, J. C.: Simplified Method for the Determination of Chlorides in Blood or Plasma, J. Biol. Chem. **45**:449, 1921.

16. Van Slyke, D. D., and Fitz, R.: The Determination of B-Hydroxybutyric Acid, Aceto-acetic Acid and Acetone in Blood, J. Biol. Chem. **32**:495, 1917.

Sugar.—All determinations were well within the normal limits, averaging 0.096 per cent.

Nonprotein Nitrogen.—One reading was slightly higher than normal, but the average was 28.1 mg. per 100 c.c. (normal, 25-35).

Chlorids.—The highest reading was 622, the lowest 404, with an average of 490.8 mg. per 100 c.c.

Acetone Bodies.—There were no acetone bodies.

Creatinin.—The highest reading was 1.91, the lowest 1.39, and the average 1.73 mg. per 100 c.c.

Urea.—The highest reading was 26.1, the lowest 1.42, and the average 17.8 mg. per 100 c.c.

Uric Acid.—The results of five examinations range from 1.4 to 2.8 mg. per 100 c.c.

The methods employed in blood analysis were the same as those used in the case of the spinal fluid, with the exception that the Folin-Wu method without modification was employed in determining blood sugar.

DISCUSSION

A study of the foregoing cases shows that when all tests on the cerebrospinal fluid are considered it can rarely be said that the fluid is entirely negative. It is true, however, that the abnormalities may be so slight as to be of little clinical significance except as evidence that a pathologic condition exists. But in approximately half of the fluids there are pathologic changes which cannot be overlooked. Foremost of these significant findings is the presence of a paretic colloidal curve. Formerly thought to be indicative of general paresis, this reaction has occasionally been found in brain tumor, encephalitis, acute alcoholism and other conditions. In this laboratory we have rarely seen it except in parenchymatous syphilitic disease of the nervous system and in multiple sclerosis. Another test appears to be of value when considered with the others: a reliable quantitative test shows the total protein of the fluid to be normal or only moderately increased, usually much less than in the various syphilitic affections of the nervous system, with which this disease is likely to be confused. The cell count is usually low—less than 10 per c.mm.—but being mostly lymphocytes, the cell picture frequently indicates a mild inflammatory or irritative process.

We may say, then, that a fluid obtained under normal or low pressure, containing a few lymphocytes, a normal amount of or only a slight increase in protein, with a negative Wassermann reaction and a paretic colloidal gold curve, is highly suggestive of multiple sclerosis. We may also say that in multiple sclerosis, although we frequently do not

obtain this combination of findings, we find some abnormality as a rule, and we must admit that the fluid is not usually entirely negative.

Is there any reason for these variable types of reaction? Analysis of the activity of the pathologic process might give the clue. Although difficult to be sure of the activity of a pathologic process from clinical observation in any disease, we are confronted in such a consideration of this disease by the fact that we do not even know what the active process looks like. In spite of this fact it seems reasonable to analyze our cases in the following manner: If there has been marked progression in the symptoms or evidence of invasion of new areas of the nervous system within six months of the time of the examination of the fluid, these cases have been considered as "progressive"; otherwise, "stationary." An analysis of this series with reference to the four tests giving abnormal findings is given in Table 2.

TABLE 2.—Analysis of Cases

	Progressive	Stationary
Total protein		
Increase (over 40 mg. per cent. when quantitated)	14	8
Normal	14	8
Globulin		
Present	17	8
Absent	17	8
Cells		
More than 10 per c.mm.	8	0
Less than 10 per c.mm.	21	16
Gold Chlorid		
"Paretic" type	16	1
"Syphilitic" type	5	2
Abnormal reaction	2	1
Negative	3	7

In this table when two or more examinations have been made on one patient only one has been recorded unless the type of reaction differed; for example, Case 11 is represented twice, Case 12 only once. The total number of cases appears to be 41 because three patients (24, 28 and 38) must be classed both as progressive and stationary types.

It is obvious from analysis of this table that total protein and globulin are not increased with certainty in either group and that no dependable guide as to the activity of the pathologic process is to be gained from these tests. The cell count is perhaps of some value in that significant increase is found only in the progressive types; however, a much larger number of fluids from actively advancing cases give cell counts below than above 10 per cubic millimeter. Pleocytosis cannot therefore be considered a reliable criterion of activity. Turning

to the gold chlorid reaction, we are struck by the large number of paretic types obtained in the progressive cases, and by the fact that only three are entirely negative; conversely, the stationary cases yield predominantly negative reactions.

In spite of the obvious inaccuracies in such a clinical and laboratory correlation, there is unquestionably some parallel between activity of the disease and pathologic findings in the fluid. While the laboratory evidence of activity of the process rests on a consideration of all tests, evaluation of these several tests shows that increase in cells and protein are less constant than the change in character of the colloidal gold curve.

Analysis of spinal fluid findings in patients examined more than once is of interest. The spinal fluids of eight patients have been thus investigated. In all no great variation in tests is noted at different times, with the exception of the gold reaction. In Cases 12 and 38 this test remained essentially the same—in the former over a period of seven months, in the latter over a period of four years. The most significant changes are seen in Cases 11 and 35, in both of which the character of the colloidal gold reaction changed materially, in the latter case during an interval of less than one month. In seeming contradiction of the conclusions reached in the foregoing, there was no obvious change in the clinical course of the disease correlative with the change in these tests. It would be of considerable interest to determine in a larger series whether spinal fluid examinations are often as variable in an individual case as is indicated in these two patients.

Three patients presenting symptoms suggestive of spinal cord tumor were examined by means of combined cistern-lumbar puncture. A comparison of the fluids obtained from these two loci at the same time is of interest in that no distinctive difference is seen; this suggests that in these cases the pathologic process is cerebral as well as spinal. The slightly greater protein content of the lumbar fluid is also seen in examination of normal persons.

Concerning our chemical examinations other than the routine tests already discussed we cannot be dogmatic. These studies were made as a matter of research, with the hope of obtaining insight into this disease from possible metabolic disturbances which might show in the blood and spinal fluid. For example, it was possible that with breaking down of myelin sheaths there might be thrown into the blood or fluid certain products of fat metabolism; yet we were unable to detect in either any trace of acetone bodies. Although the normal values of the various substances tested for in the fluid are not as yet certain, judging by the few reports in the literature and by our own work, we must regard the figures obtained in multiple sclerosis as probably within normal limits. Compared with the figures in normal blood, we also find no radical departure in this disease.

CONCLUSIONS

The spinal fluid findings in thirty-eight cases of multiple sclerosis, together with certain blood examinations in a number of these, are given.

There is no single fluid test of paramount value in the diagnosis of multiple sclerosis. However, correlation of all tests ordinarily performed on the spinal fluid indicates that it is seldom entirely normal, and that in 50 per cent. of the cases of this series findings unusual in other diseases were obtained. This group of findings, which we consider important, is as follows: fluid of normal appearance, obtained under normal or low pressure as registered by the manometer, showing a slight increase in cells (lymphocytes and arachnoid mononuclears); total protein normal or only slightly increased; globulin, a slight trace or absent, and a paretic colloidal gold curve with a negative Wassermann reaction.

Correlation with the clinical picture suggests that this type of fluid indicates a progressive stage of multiple scloresis. Conversely, normal or nearly normal fluids were found primarily in patients in whom no clinical progress had recently been apparent. Results of certain chemical studies designed to show disorders of metabolism in this disease, performed on blood and spinal fluid, were normal.

AN ADDITIONAL CONTRIBUTION TO THE SYMPTOMATOLOGY OF EPIDEMIC ENCEPHALITIS *

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At the request of the organization committee, we have reviewed our cases of epidemic encephalitis occurring during the past year, with a view to the discovery of novel symptomatology or disease incidence which might be of either diagnostic or pathologic interest. It has always, of course, been clear that an infection flung far and wide through the nervous system would inevitably produce in different persons extraordinarily diverse clinical pictures. In epidemic encephalitis the diversity observed becomes greater with increased experience, and we have been fortunate enough in the neurologic department of Bellevue Hospital to find many examples of disease incidence in the sensorimotor system both central and peripheral, and, we believe, in the vegetative nervous system as well.

We have grouped cases in this paper under the headings: spinal types, disturbances of metabolism, disorders of motility and symptoms evidencing impairment of the vagosympathetic mechanism. The cord syndromes which have been described heretofore are confined to cords having an affection of the ventral horns and those in which a transverse softening has taken place. It becomes certain, however, that more discrete destruction can occur in the cord giving rise to clear-cut pictures of transient syringomyelia.

One such case was that of a young woman with general constitutional symptoms of infection, who, after having violent shooting pains in the left arm, experienced paresis of the arm, together with pyramidal weakness of the left side of the body and loss of temperature and pain sensibilities over the right side of the trunk between the spinal segments—the fifth cervical and the ninth dorsal. The left hand became swollen and succulent in appearance, indicative of vasomotor stasis, due to the lesion having involved not only the ventral horns and crossed sensory paths but the intermediolateral tracts as well. This grave picture was removed in four months, when the patient's health had been entirely restored.

Our second example was the case of a young man who one of us at first thought had a case of conal tumor. After two weeks of acute insomnia, he developed weakness in dorsiflexion of both feet and abduction of the thighs and clear-cut loss of pain and temperature senses in the skin areas served by the

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* From the Neurological Department, Bellevue Hospital.

lumbar and first sacral segements. The ankle reflexes were abolished and the knee reflexes depressed. The right plantar reflex was of extensor type. There were myoclonic movements of one leg. Entire recovery took place within three months.

DISTURBED VEGETATIVE FUNCTION

We believe that the significance of disturbed vegetative function in encephalitis can hardly be overstated; not only are such cases difficult to diagnose, but some of them may furnish valuable data for a future comprehension of neurotic and psychotic phenomena on a physical rather than on a purely emotional or psychic basis.

H. G., aged 21, served as a private in the United States Marines during the war and was supposed to have disintegrated mentally after an alleged attack of influenza in London, during the month following the armistice. He was placed in a hospital for mental diseases for about eight months after his return home. The clinical picture seen in the spring of this year was sufficiently confusing; a young man of splendid physique, carried his height of 6 ft. 2 in. (1.87 meters) with a pronounced stoop, an acquisition of his illness. Despite the exclusion of the possibility of syphilitic infection, the pupils were distinctly sluggish to light, the right side of the face definitely flattened in its creases, and there was a fine jelly-like, but most definite, nystagmus on lateral conjugate deviation of the eyes to the right or left. There was pronounced tremor in the extended hands. He had lost over 30 pounds (13 kg.) since his illness; but except for the absence of the abdominal reflexes, great increase in the arm, knee and ankle reflexes and involuntary shivering movements of the pectoral muscles, nothing more of pathologic interest could be made out in the sensorimotor system. He suffered, however, from severe nocturnal insomnia, rarely sleeping more than two hours before dawn, after which he would grow drowsy and might sleep three or four hours before noon. Whether he slept or not, during the first part of the day he was utterly inert and exasperated by his inertia. He had the utmost difficulty in accomplishing simple acts, such as shaving, dressing or bathing. He agonized for hours in futile efforts to write a short note or keep an important engagement. In his mental attitude there was not a trace of negativism; he desired passionately to do those things which he could not do at that time, but which later in the day he often could do with relative ease. There seemed to be a distinct resemblance between his inability to perform acts to the completion of which he was urged by will only without the stronger adjuvant of emotion, and the palsy of purely voluntary movements in midbrain encephalitis of the parkinsonian type—palsies so often abolished by affective stimulation. He complained frequently of "numb attacks," during which he felt very cold and during which he shivered and his teeth would chatter like a man with a rigor. During these attacks, even in July weather, his rectal temperature was always subnormal, on several occasions being 97 F.; and on his skin were large patches of goose-flesh which covered a third of the body area at a time and which, under observation, changed their position like a breeze over still water.

In the same general period but not necessarily and indeed rarely at the same hours, he had attacks of disturbed breathing rhythm of from a quarter to half an hour's duration. During these attacks he felt as though he could not fill his lungs with air, and he breathed with all his accessory respiratory muscles

from fifty-six to sixty-four times a minute. At other times he experienced what seemed like a spasm of the laryngeal muscles and breathed more and more stertorously and ineffectively so that the lips were cyanosed and the eyes protruded. Phenomena such as these have appeared at times in hysteria, and various physicians had considered them hysterical in this case. This explanation, however, would not account for the patient's abnormal thirst for ice water. He consumed for a period of eighteen months, between thirty and forty quarts of water every twenty-four hours and had proportionate polyuria.

An analysis of the initial illness in December, 1918, which he had always considered influenza, revealed the only symptoms to have been severe headache and intense sleepiness by day and by night. Two negative features of value, however, were that he had had no feeling of fever and that he had never reported sick to a medical officer. It is highly unlikely that this would be true of any youthful patient with the influenza which was prevalent in London at the end of 1918. Furthermore, after three or four weeks sleepiness disappeared during the night time and was only present by day, a reversal of the sleep mechanism sufficiently familiar to all students of epidemic encephalitis.

This patient's symptoms during the last eight months have gradually improved so that now he is almost normal, with little or no morning inertia, no difficulty with respiration and no rigors, and diabetes insipidus has been reduced to an intake of only 3 quarts of water a day. It is possible that this happy result has been assisted by the constant administration of scopolamin during the last four months of his illness; on this subject more will be said later.

A case brought under our observation recently has afforded us a fortunate diagnostic corroboration in that this strange syndrome is to a large degree duplicated. In this second instance, the patient, a boy of 14 years, had a similar polydypsia and polyuria with tremors in the upper extremities, excessive salivation and similar distressing paroxysmal attacks in which breathing was exceedingly rapid, labored and difficult. At these times there was great emotional distress and suffering. In this boy, acute encephalitis occurred in January, 1920, with visual disturbance, diplopia, fever and excessive insomnia; this was followed for many months by apparent recovery and was then gradually succeeded by a rhythmic incessant cough and thereafter by the distressing symptoms mentioned.

Another example of seriously deranged metabolism was the case of J. D., a well-developed young man of 24, who in the late spring of 1920 had an acute illness accompanied by headache, diplopia, diarrhea and nervousness. Shortly afterward an increasing desire to sleep and difficulty in the use of the right arm, leg and right side of the face appeared. A month later excessive thirst and polyuria developed, and at this time sugar was found in the urine. A low carbohydrate diet for two months improved the glycosuria and entirely relieved his thirst and polyuria. As these symptoms waned a gradually increasing slowness of speech and movement began. In Bellevue Hospital in July of this year, he presented a typical unilateral pseudoparkinsonian syndrome without any evidence of diabetes mellitus.

Another patient, a woman, aged 28, developed severe hypertrichosis of the face and arms following encephalitis. Great increase in body weight has been a fairly common sequel of epidemic encephalitis. It happens that this disturbance of metabolism was seen in our series only in female patients. One patient within a year gained over 100 pounds (45 kg.). She eventually died, probably of myocarditis. Among five other patients, gains of from 40 to 70 pounds (18 to 31 kg.) were noticed. The blood sugar was found to be normal in two instances, but in a woman, aged 52, with an increase in weight of 60 pounds (27 kg.), sugar tolerance was below normal. The climacterium as a contributing factor in the increase in weight could be excluded in all but one of our cases.

DISORDERS OF MOTILITY

Certain disorders of motility, some of which may not be new to other observers, we feel to be worthy of report. In particular, we feel that stammering, rhythmic movements, breathing irregularities and eccentric stations may be attributed to disturbance of the toning mechanism of the muscles.

In five patients, all with a pseudoparkinsonian syndrome, stammering developed as a sequel to their illness. In one of these cases the disorder accompanied a severe relapse, precipitated by a fright occurring two months after the onset of encephalitis. In the other instances, stammering appeared from three months to two and a half years after the first symptoms and without any psychic trauma. Rhythmic movements were observed in three patients. A. B., aged 28, had from the onset of her illness bilateral tremor of the masseters, associated with rhythmic muscular action, which gave a champing movement of the jaws. This was constant during the waking hours, and, with the immobile facies and unwinking stare, resembled remarkably the breathing movements of a fish.

In H. B., aged 32, the left side of the face suddenly began to twitch three months after an alleged influenza in the winter of 1919. The movement involved only the mouth, and did not cease or spread, but gradually the contractions became stronger. E. P., aged 19, had a similar affection from the onset of her illness.

In all these cases the movements occurred about once a second, were not under control of the will or varied by attention or emotion and could not be inhibited by any voluntary use of the involved muscles. The absolute rhythm of these movements distinguishes them, to some extent, from habit spasms, in some of which, however, there may be a striatal origin; indeed, we think many cases of hysteria may be in essence a retreat from a cortical to a more primitive reflex level of motor expression.

Breathing spasms were seen twice. One patient, E. P., just mentioned, had had from the beginning very irregular breathing—both in depth and rate—accompanied by curious noises which occurred only during sleep. S. J., fifteen months after apparent total recovery from encephalitis, had a parkinsonian relapse, accompanied by attacks of rapid deep breathing. These increased in frequency and at length continued through the waking hours, causing much fatigue. Emotion would initiate them, but when started they could not be stopped until their course was run—usually in a minute or two. There was never any feeling of dyspnea, but a sensation that the lungs could not be filled, and he had a desire to expand them as much as possible.

A patient, during the course of encephalitis which began with headache and spinal root pains, soon followed by a hemiplegia and later by various cranial nerve involvement, developed recurrent vomiting which persisted for three weeks. Several times a day, with or without food in the stomach, expulsive movements occurred; we speak of the case at this point in the belief that the vomiting was probably in morbid process analogous to the rhythmic movements and breathing spasms just described, and also analogous to the hiccup seen in certain cases of encephalitis.

Anteropulsion of the trunk was seen in a boy of 12. Another boy, aged 15, maintained when sitting or standing, a deviation of the trunk to the left. Neither patient ever fell. At a certain point the pull would cease and the attitude would be maintained. No cerebellar symptoms were found in either case.

Two parkinsonian patients developed bulbar palsy with lingual and pharyngeal atrophy nine months after the initial illness. Of these, one improved, the other died.

Limitation of parkinsonian symptoms to the upper extremities and the face was observed twice. Another patient presented curious irregularities of posture, owing to acute spasm of particular muscle groups. These phenomena lead us to speculate on the possibility that individual centers in the corpora striata may govern individual spinal segments.

We have the following evidence of disturbance in the vagosympathetic mechanism: In nine of fifteen cases tested there was a strongly positive oculocardiac reflex. Ocular pressure stopped the pulse absolutely in four patients—in one for a period of twenty-eight seconds after pressure was relieved. The pulse rate dropped 15, 20, 35 and 40 beats a minute, respectively, in four other cases. The ninth patient showed a pulse rate increased by twenty beats a minute. The other six patients gave no reaction to ocular pressure. The degree of reaction in a given case could not be foretold on a basis of the general clinical picture and had no relation to the patient's ordinary pulse rate. The percentage

of strongly positive oculocardiac responses is much higher in epidemic encephalitis than in numerous control tests made on a variety of other cases.

EXOPHTHALMOS

In twelve patients we observed exophthalmos. This varied in degree, was most marked in the definite parkinsonian cases, and was accompanied by a diminution of the wink reflex. It is perhaps noteworthy that this exophthalmos, a sympathicotonic sign, was often present in patients who were vagotonic, as judged by a strongly positive oculocardiac reflex.

THERAPEUTIC RESULTS

A few words on the result of treatment of residual cases may be of interest. It has seemed to us that medication should be based on a drug or drugs acting chiefly on the vegetative nervous system. The problem is a broad one and is complicated by the fact that in any given case of encephalitis the symptoms are not characteristic of damage to either the autonomic or the sympathetic system alone. There is instead a confused picture evidencing functional impairment of both divisions of the vegetative nervous system. It is possible in this paper to give only a mere sketch of our therapeutic results, which will have to be corroborated by further observations before any definite conclusion can be reached.

Thyroid and pituitary substances have no effect on residual encephalitic symptoms. Epinephrin, given to three patients in 20 minim subcutaneous doses of 1:1,000 solution, increased the pulse rate 50 per cent. and increased the rigidity of extremities for a period of two hours. In three controls the maximum pulse increase was 15 per cent. Nicotin in doses of $\frac{1}{30}$ grain (0.002 gm.) subcutaneously, did not affect the pulse rate, but did decrease rigidity for a period of from ten to fifteen minutes. Atropin, when used in large doses, increased rigidity and made the patient subjectively worse. Scopolamin, doses of $\frac{1}{100}$ grain (0.006 gm.) by mouth three times a day over a period of several days, has produced in about half the cases in which it was used a lessening of rigidity; it has restored facial mobility and has made the patients generally more comfortable. Gelsemium—the fluid extract—in doses of 7 minims (0.42 c.c.) three times a day or gelseminin hydrochlorate $\frac{1}{30}$ grain by mouth three times a day, has an effect similar to that of scopolamin in the same proportion of cases. These favorable effects of gelsemium persist as long as it is used; in one case these effects lasted for a period of over three months.

In perhaps a quarter of the cases, cumulative drug effects have been observed. These consist of heaviness of the eyelids, diplopia and, at times, a feeling of languor and confusion. They disappear within

twenty-four hours of the withdrawal of the drug, and they were alarming only once. In this case fluid extract of gelsemium, 5 minims (0.3 c.c.) three times a day, had been used for six days, and then scopolamin 1/100 grain (0.0006 gm.) given subcutaneously. Within five minutes after the injection of the latter, the patient became confused, weak to the degree that lying down was necessary and flushed of face, with rapid pulse and dilated pupils. Her severe parkinsonian tremor absolutely ceased. This state lasted four hours. Scopolamin alone by mouth or subcutaneously never had any such effect on this patient. The situation was reproduced, and the same cumulative phenomena recurred. These observations suggest a synergism between scopolamin and gelsemium. The action of gelsemium on true paralysis agitans cases was studied. It produced the same relief which scopolamin has long been known to give. Thus both in true paralysis agitans and in postencephalitic pseudoparkinsonian disease, gelsemium seems to be ameliorative in approximately half the cases. While both scopolamin and gelsemium, according to Cushny, act by depressing the central nervous system, gelsemium has a distinct advantage over scopolamin in that it can be used for an indefinite time and has none of the dangerous concomitant effects of the latter. Why scopolamin, "which produces a sensation of fatigue and drowsiness" and after a dose of which "the patient moves about less and speaks less," [1] can relieve symptoms of the same sort in encephalitis, we cannot yet answer.

Our most striking therapeutic result, however, was obtained in January, 1921. A woman of middle age who had been unable to articulate, chew or move the arms or legs on volition—so intense was the parkinsonian spasm—after a suppository of belladonna, was able to talk fluently, move quickly and with grace, and express emotion easily by gesture and facial expression. Congealment of function gradually returned, but temporary dramatic amelioration has always been possible by the rectal use of belladonna in tolerance dosage.

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1. Cushny: Pharmacology and Therapeutics, Philadelphia, Lea & Febiger, 1910, p. 295.

EXOGENOUS CAUSES OF MULTIPLE SCLEROSIS*

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My report has nothing to say concerning possible endogenous causes, and it also excludes certain exogenous etiologic agents such as direct bacterial infections or parasitic invasions, which are to be dealt with by others. The possible exogenous causes that I have to consider are: (1) the influence of earlier infections; (2) the influence of intoxications; (3) thermal and electrical influences, and (4) trauma.

With the aid of Dr. Caroline Latimer and Miss C. J. Smith, I have analyzed forty-four cases from my private practice and from the records of the Johns Hopkins Hospital, all studied between 1905 and 1921.

INFECTIONS

Pierre Marie of Paris has suggested, and the suggestion has been favorably entertained by various neurologists, that multiple sclerosis might be a sequel of various infectious diseases. It has been observed in a certain number of cases, not in many however, that the symptoms of multiple sclerosis began to appear soon after the occurrence of an infectious disease. Possibly in some of these cases it was a disseminated encephalomyelitis rather than a true multiple sclerosis that was dealt with. Granting, however, that occasionally true multiple sclerosis has occurred soon after an infection, this relationship may have been purely accidental. Unless the infection and the onset of multiple sclerosis are chronologically closely related, there could be little justification in considering the multiple sclerosis as a sequel of the infection. It has been fairly well established that multiple sclerosis may undergo exacerbation from intercurrent infection, and it seems probable that the instances in which multiple sclerosis has been supposed to begin after an infection have been instances in which the disease in reality existed unnoticed before the infection, its so-called "beginning" having been called forth by the infection.

If we take into account only cases in which an infection has preceded the apparent onset of multiple sclerosis by, say, two or three months, not longer, the statistics in the literature indicate that only from 3 to 5 per cent. of the cases recorded show such a temporal connection with infection (Berger; Hoffmann). In this country Woodberry (1919) has emphasized the co-existence of chronic tonsillar infections; Gill and Bassoe call attention to the frequency of both tonsillar and dental infections.

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In the cases that have occurred in my own practice and in the Johns Hopkins Hospital, there was a history of one or another infection shortly before the onset of the symptoms of multiple sclerosis in five of the forty-four cases; these infections included gonorrhea (1), tonsillitis (1), nasopharyngitis and otitis (1), abscesses of the teeth (1), and influenza (1). This is a meager showing, and I attach no significance to it. In the distant past of the persons whose cases were analyzed, childhood infections were as common but no commoner than in other patients; five of the forty-four patients had had typhoid fever, five tonsillitis, five abscesses, four scarlet fever, two syphilis and one erysipelas. It will be seen that there is nothing striking about such a record of earlier infections.

Since the outbreak of epidemic encephalitis in 1917 the occurrence of a certain number of cases in which the disease became chronic, with exacerbation, has been noted, and doubtless many have wondered whether or not some of these might follow a course similar to that of true multiple sclerosis or possibly might even be identical with it. In the few necropsies that have been made on such cases, however, the lesions found have not been those of multiple sclerosis.

INTOXICATIONS

It was thought by Oppenheim that mineral poisoning, especially by lead, arsenic and tin, might be responsible for the origin of multiple sclerosis, and von Jaksch believed that poisoning by manganese could give rise to a clinical picture resembling multiple sclerosis if not identical with it. Undoubtedly multiple sclerosis occasionally occurs among workers in metals, and some of the European neurologists have drawn a part of their material from among such workers. But when we consider the total number of cases of multiple sclerosis, a history of poisoning by metals is rare among them, so rare that we can certainly exclude this form of poisoning as a principal etiologic agent. Multiple sclerosis is probably just as common in women as in men, or nearly so, and women are not exposed to metal poisoning. Again, in the majority of cases the disease begins in early life often at a period before the patients could have been subjected to metal poisoning from their occupations. Further, it is scarcely conceivable that the successive exacerbations that are characteristic of the disease can be explained on the ground of a succession of metal poisonings. In my series of forty-four cases, a history of metal poisoning was found in none.

Other poisons incriminated include alcohol and carbon monoxid. Jelliffe mentions alcoholism in 8 per cent. of his cases, a larger incidence, however, than is found in most statistics. Among my forty-four cases there were only two patients who used alcohol to excess; the majority were total abstainers. When one recalls the enormous number of cases

of alcoholism formerly seen and how rare it was to see multiple sclerosis in an alcoholic addict, it is improbable that it could be other than a predisposing or exacerbating factor. The same may be said of carbon monoxid poisoning. Disseminated lesions throughout the brain and spinal cord may occur in carbon monoxid poisoning, but these lesions do not appear to be identical with those of multiple sclerosis.

Dr. A. L. Skoog, of Kansas City, Mo., writes me that he has studied a painter who gave a positive history of intoxication by "volatile oils." None of our patients gave such a history.

In our Baltimore cases there were no intoxications of any sort recorded except intestinal stasis, and this feature was no more common than in the average of patients not suffering from multiple sclerosis.

THERMAL AND ELECTRICAL INFLUENCES

In some of the patients with multiple sclerosis one finds a history of heat stroke, of lightning stroke or of exposure to cold and wet. But such instances are rare, and the hypotheses that have been put forward to explain them (reflex contraction of vessels in the central nervous system due to cold; chemical changes in hemoglobin brought about by thermal influences) seem forced. Krafft-Ebing reported thermic injury in no less than forty of 100 patients. Otto Marburg saw a patient whose clothing, suddenly wet, froze on him; six days later he began to have visual disturbances due to retrobulbar neuritis, after which the typical picture of multiple sclerosis developed. Most critical observers express the opinion, however, that these thermal influences are not the causes of multiple sclerosis but, at most, are injuries that cause an exacerbation of an already existing disease. In our forty-four cases, the analysis does not reveal a single instance in which there had been electrical injuries, thermal injuries, or marked exposure to cold or wet.

TRAUMATISM

Patients with chronic nervous disease are prone to incriminate trauma, physical or psychic, as causative agent. Similarly, multiple sclerosis is not infrequently attributed to traumatic causes. It has been assumed that the trauma injures the blood vessels, does harm by violent commotion in the cerebrospinal fluid or by concussion causing molecular changes in the nerve substance, or by tearing lymph spaces with resulting necrosis in the parenchyma. No one has, however, been able to reproduce the lesions of multiple sclerosis through experimental traumatism to animals. If one adheres to the requirements laid down by K. Mendel, the incidence is small. Mendel laid down as necessary conditions: (1) direct injury to the skull or spine or violent shaking of the same; (2) exclusion of every other cause; (3) demonstration of

complete health before the trauma, and (4) demonstration of a definite temporal connection between the appearance of the first symptoms of the disease and the accident. The incidence when these conditions are regarded varies according to different authors—Schultze, 8 per cent.; Berger and O. Marburg, 9 per cent.; Jelliffe, 12 per cent.

It must be remembered that injuries often occur in multiple sclerosis as a result, rather than as a cause, of the disease, and when multiple sclerosis appears to develop after trauma careful inquiry will often show that symptoms of the disease had been present earlier. It does seem certain, however, that latent multiple sclerosis may suddenly become manifest after a severe trauma (either physical or psychic) and that manifest multiple sclerosis may undergo marked exacerbation after trauma.

In our forty-four cases, eleven patients gave a history of physical trauma of one or another sort, and three gave a history of nervous and mental strain. In most of the instances, however, the trauma had occurred long before the onset of the illness; in only three cases did it occur within a year of onset. Three of the female patients stated that the onset and progress of the disease seemed to be related to child-bearing.

CONCLUSIONS

If multiple sclerosis is a disease entity due to a single cause that acts in early life, it may be due to some specific infection, but the evidence available is strongly against its being caused by any of our well-known infections, by any ordinary intoxication (organic or inorganic), or by electrical, thermal or traumatic influences. If the exogenous factors mentioned play any rôle at all in the etiology of the disease, they must act either as predisposing influences for the true cause or as aggravators of a disease already started by the true cause.

MULTIPLE SCLEROSIS

FROM THE STANDPOINT OF GEOGRAPHIC DISTRIBUTION AND RACE *

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The results of the tabulation of multiple sclerosis as one of the defects found in drafted men are plotted on the accompanying map. It shows that the maximum rate for this disease was found in Michigan and Minnesota, in which there were eighteen persons with this disease per 100,000. The Michigan rate is based on six cases so diagnosed by local boards and on nine at Camp Dodge. Excepting Delaware and the District of Columbia (whose rates depend on one and two cases, respectively), the next highest ratio is that for Wisconsin, fourteen per 100,000, where five cases were found by local boards and six by examiners at Camp Grant. That these states with a high ratio for multiple sclerosis are adjacent states, bordering on the Great Lakes, is of great interest. Since examinations were made at three different camps, the result cannot be ascribed to the idiosyncrasy of a neuropsychiatric examiner at one camp (Fig. 1).

The nearest approach to the distribution of multiple sclerosis found in any other diseases is in goiter, exophthalmic goiter, chorea, varicose veins, varicocele and allied diseases and various heart diseases and defects. The cardiovascular diseases are associated with the tall stature of the men living about the Great Lakes—largely Scandinavians. The resemblance between the distribution of multiple sclerosis and chorea is considerable, except that chorea is abundant also in Texas, Mississippi, Missouri and the states of the North Atlantic coast and of the eastern slopes of the drainage basin of the Ohio River; that is, high rates of chorea are more widespread than of multiple sclerosis. It is rather interesting that especially high rates for chorea, as for multiple sclerosis, are found, outside the Great Lakes region, also in the states of Washington, Mississippi and Maine.

The resemblance of the distribution of multiple sclerosis to that of simple goiter is somewhat striking. In both diseases comparatively few cases are found south of the Ohio River. The maximum rate is found in Michigan, Wisconsin and the extreme Northwest.

Various hypotheses are suggested for these facts. One is that some race inhabits the Great Lakes region and the state of Washington that

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* Presented before the Association for Research in Nervous and Mental Diseases, December, 1921.

is especially subject to multiple sclerosis as well as goiter, chorea and cardiovascular defects. One thinks of the big Swedes that live in these parts of the country. Probably the cardiovascular defects are associated with the tall stature of men from these localities. The goiter is supposed to be due to the absence of iodin in the potable waters. Whether or not chorea and multiple sclerosis are especially common among Scandinavians cannot be definitely asserted. The matter is considered later in this paper. It is, of course, possible that in the rapid diagnosis of local boards and camps some cases of chorea may have been diagnosed as multiple sclerosis and vice versa.

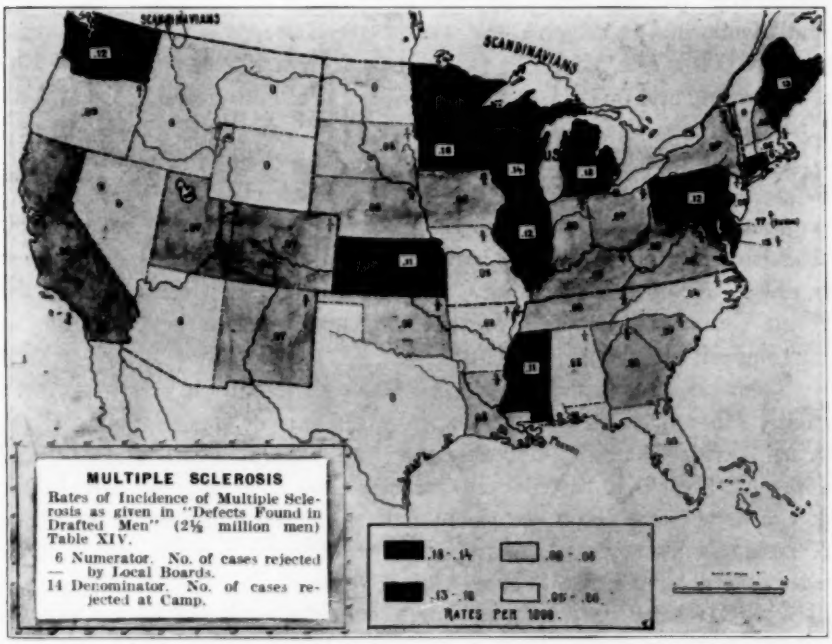

Fig. 1.—Map of the United States showing by states the varying density rate of multiple sclerosis. "Dodge," "Grant," and "Custer" in the Great Lakes region are the names of camps at which the drafted men from those localities were mobilized. (From "Defects Found in Drafted Men.")

RATE OF MULTIPLE SCLEROSIS IN URBAN AND RURAL POPULATION

For the United States as a whole, the defect rate found in the draft was, for multiple sclerosis, 10 per 100,000 of the population examined. The urban rate was 12 per 100,000 and the rural rate 8 per 100,000; thus the urban rate was one-half greater than the rural rate. For four large cities (combined) the rate was 14; the rate for each city was: Philadelphia, 23; Boston, 16; New York, 13, and Chicago, 11.

SECTIONS AND GROUPS OF SECTIONS

The rate per 100,000 men examined in the draft is shown in Table 1.

TABLE 1.—RATES PER 100,000 FOR MULTIPLE SCLEROSIS ("DEFECTS IN DRAFTED MEN")

For southern, prevailingly *white* agricultural communities	7
For southern, prevailingly *colored* agricultural communities	6
For northern agricultural communities, prevailingly native white	8
For northern agricultural communities, prevailingly foreign	10
For mining sections	7
For maritime sections	10
For mountain sections	2
For the "mountain whites" of the South	7
For Indian sections	1
For Scandinavian sections	16
For German and Austrian sections	10
For Finnish sections	29
For French-Canadian sections	8

The high ratios found in Scandinavian and Finnish sections are probably significant. However, both Finnish sections are in the Great Lakes region, which is a region with a high rate of multiple sclerosis.

RACIAL DISTRIBUTION

In 1902, the incidence of multiple sclerosis in New York City among patients with nervous diseases was considered low. The rate was from 2 to 7 per 1,000, except that Dr. Onuf found, among 500 to 600 cases, 14 per 1,000, and Fraenkel found 18 per 1,000 among Jews at the Montefiore Home.

In 1903, Taylor and Myers, in Boston, found only 1 per 1,000 among nearly 10,000 nervous cases. They called attention to the great difficulties of diagnosis. If patients with certain ataxic paraplegias, diffuse degenerations and spastic paraplegias were included, the rate would be increased to 4 per 1,000.

Van Wart, in 1905, on the basis of 500 nervous cases in New Orleans, found a rate for multiple sclerosis of 44 per 1,000 and concludes that in Louisiana and the surrounding states multiple sclerosis is an extremely frequent disease. But this may well be due to the idiosyncrasies of the examiners. Perhaps a prevailing tradition is responsible for the high rate for this disease in Mississippi at the time of the draft.

For other countries the rate is said to be much higher than the 2 to 7 per 1,000 in New York City. Thus the Bramwells (1903, 1915) find a rate first of 20, and later of 32, in Scotland and the North of England. Williamson is said (Collins and Baehr, 1914) to have found a rate in Manchester of 27 per 1,000 and the National Hospital for Paralyzed and Epileptic in London of 60 per 1,000 "nervous cases";

but in this hospital the patients with nervous cases were a more rigidly selected lot than in many of the other instances, so that multiple sclerosis formed a larger proportion of the population than in other hospitals. According to Jelliffe (1904), Jolly of Berlin found 8 per 1,000 multiple sclerotic patients among nearly 10,000 patients with nervous diseases; and Sanger of Hamburg about 10 per 1,000.

Various authors, such as Jelliffe (1904) and Collins and Baehr (1914), give statistics concerning the racial constitution of patients with multiple sclerosis. But in a country whose racial composition changes so rapidly it is difficult to compute satisfactory racial rates. Also, there is reason for thinking that there is a racial selection for particular clinics. Thus, private patients are more likely to include an excess of native Americans and Germans, and the hospital clinics of the later immigrants. The excellent provision made for Jewish patients in special hospitals for that race diminishes the Jewish rate in the general hospitals.

TABLE 2.—Rates of Various Foreign Nationalities in New York and Among Patients with Multiple Sclerosis

1	2	3	4	5
Name of Nation	Number in Greater New York, 1920, per Thousand	Proportion of Total Foreign-Born Population of 1,990,000	Number of Cases of Multiple Sclerosis Listed in the Four Hospitals	Proportion of Entry of Column 4 to 70 Foreign-Born Patients
Russia	480	24.1	9	12.9
Italy	389	19.6	11	15.7
Germany	194	9.8	12	7.2
Ireland	203	10.2	8	11.5
England	71	3.6	5	7.2
Sweden	33	1.7	3	4.3
Norway	24	1.2	3	4.3

Miss Louise A. Nelson has ascertained the birthplace of seventy foreign-born patients with multiple sclerosis from the records of Montefiore Home, Neurological Institute, St. Luke's Hospital and Post-Graduate Medical School. According to the bulletin of the United States Census Bureau, the number of foreign-born persons per 1,000 in Greater New York for the leading countries is as given in column 2, Table 2. The proportion that each number makes of the 1,990,000 foreign-born persons for the seven leading nationalities is given in column 3. The number of cases of multiple sclerosis in these same nationalities found by Miss Nelson is given in column 4. The proportion that each is of the seventy foreign-born patients with multiple sclerosis is given in column 5. Were the patients distributed among the nationalities in the same ratio as the whole foreign population, columns 3 and 5 should be closely similar. Actually they show striking differences. Thus the number of cases among the Russians and Italians are far below expectation. The number of cases among the Irish are

slightly above expectation; the English and Germans have about twice as many cases of multiple sclerosis as expected; Sweden has about 2.5 times and Norway about 3.6 times as many cases as expected. Without laying any stress on the exact multiples, we have relatively more Scandinavians with multiple sclerosis in the hospitals named than we would expect were patients of all nationalities equally likely to go to these hospitals and were the rate of incidence the same in all nationalities. While we cannot assume the first to be true, still there is no obvious reason why it should not be approximately true. If this be granted, it would follow that there is probably an exceptionally high incidence of multiple sclerosis among Scandinavians. Incidentally it may be said that Jelliffe's figures also seem to show that there are more Scandinavian than Russian patients in a New York City clinic. When we recall that in the draft statistics the rate for multiple sclerosis is high in states with a large proportion of Scandinavians, it does not seem unwarranted to suggest that the Scandinavian race may be especially subject to this disease.

It is only right to add that a visit to the Swedish Hospital, Brooklyn, since the foregoing was written, did not reveal any cases of multiple sclerosis there nor listed on the records of the hospital. However, this hospital does not receive many nervous cases.

The negro race is not immune from this disease; although, as indicated by Table 1, it—including mulattoes—is probably less subject to the disease than the white race. Miura (1911) states that the disease is infrequent in Japan, while amyotrophic lateral sclerosis is common.

HEREDITY

If there is any racial tendency in multiple sclerosis in the strict sense of the word, there is an hereditary factor. Usually inquiry of the patient elicits no evidence of the disease or any similar disease in other members of the family. In other cases positive evidence of recurrence in the family is obtained. Multiple neurofibromatosis is hereditary; hence, if multiple sclerosis is a primary hyperplasia of the glia, it might well be hereditary also.

Since it is impossible at this time to make such an assertion, it will suffice to consider the pedigrees of a number of families containing one or more cases of diseases regarded as probable multiple sclerosis.

The most famous instance is that first described by Pelizaeus (1885), and continued twenty-four years later by Merzbacher (1909). This pedigree chart (Fig. 2) is shown herewith (from Arch. Rassen-u. Gesellsch.-Biol., 1909). Some authors doubt the diagnosis in this case and would classify the condition as an hereditary type of "cerebral diplegia."

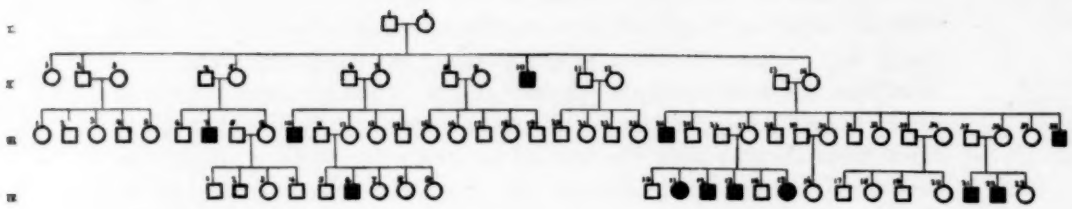

Fig. 2.—Eickhold pedigree of multiple sclerosis of Tübingen and vicinity, Germany. The squares represent males and the circles females. The dark symbols indicate those affected with the disease. The earliest generation is represented by the top line. Merzbachers, Arch. Rassen u. Gesellsch., Biol. VI, 1909.

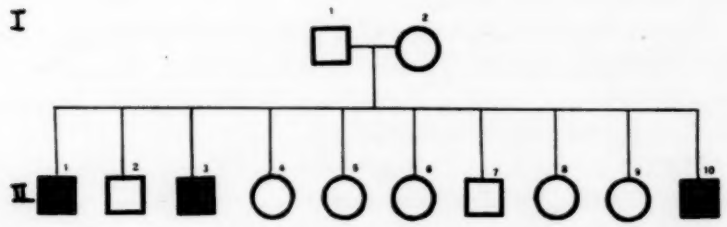

Fig. 3.—Pedigree of multiple sclerosis, showing three sibs affected. Pauly et Bonne, Rev. de méd., Paris, 1897.

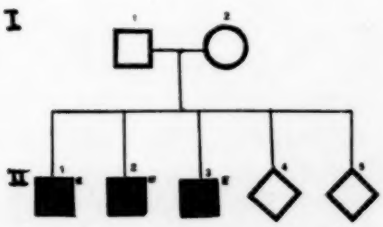

Fig. 4.—Pedigree chart of parents and their children; a Bohemian family. The three dark symbols represent three sons with multiple sclerosis and epilepsy. There are also two normal children and two who died in infancy. Abrahamson, J. Nerv. & Ment. Dis. **33**:200, 1906.

Another considerable pedigree is contributed by Batten and Wilkinson, 1914. As in Merzbacher's report, chiefly males are affected, and the tendency is passed on by mothers who are not themselves affected. This reminds one of the ordinary sex-linked type of heredity. Numerous hereditary data for the disease have been collected by Klausner (1901) and Röper (1913).

Recurrence of the disease in two generations is not common in typical multiple sclerosis, and when it does occur, the mother and child are usually affected. Such is the case of Eichhorst (1896). A woman

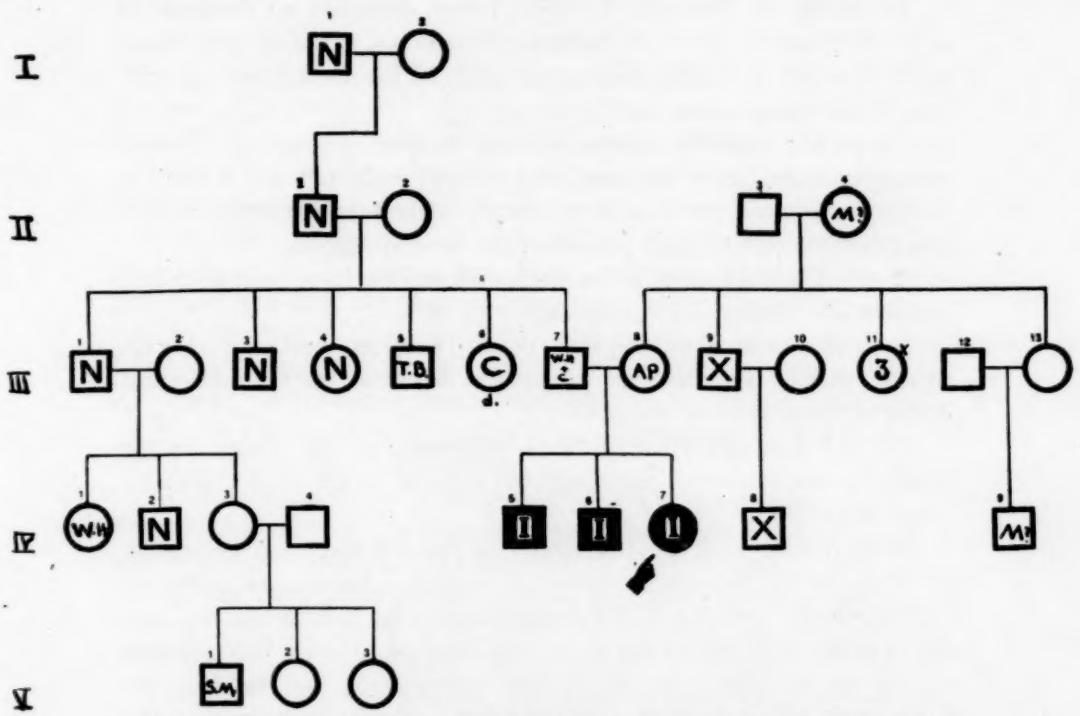

Fig. 5.—Pedigree chart of multiple sclerosis in case of R. J., Central Islip State Hospital. *N* indicates normal; *M?* mentally questioned; *AP*, died of apoplexy; *T.B.*, tuberculosis; *C*, cancer; *W.H.&C.*, weak heart and cardiac disease; *S.M.*, spinal meningitis; *I*, insanity; *X*, little known; dark symbols, multiple sclerosis.

first noticed weakness in the legs, which finally no longer would hold her, and tremor set in. Speech became disturbed and scanning. There was horizontal nystagmus. The optic papillae looked pale. Intention tremor developed. Multiple sclerosis all along the cord was found at necropsy. Her son showed tremors shortly after birth in 1879; he developed weakness of the leg in 1887, then diminished vision, nystagmus and scanning speech. Necropsy revealed sclerotic changes in the

cord only, as in the mother. Groups of atrophic nerve fibers were found, especially in the anterior roots. The mother had three normal children.

Klausner (1901) gives an account of nervous "heredity" in thirty-one of his patients. In one (No. 10) the arms and legs of the mother had been paralyzed for sixteen years, and the daughter began to have symptoms of multiple sclerosis at 18 years of age.

In one of Röper's (1913) cases a mother had paralysis agitans and two sons had typical symptoms of multiple sclerosis.

According to Bramwell (1915), Lenot described an instance in which both mother and child had multiple sclerosis. One of the patients at the Montefiore Home, November, 1921, had a similar history, with paralysis in the grandmother.

Cestan and Guillain (1900), describe the case of a boy of 15 years with paraplegia, highly exaggerated knee and ankle reflexes, a positive Babinski sign, but no speech or macular defect or intention tremor. His father and eldest sister presented the same symptoms.

Cases of multiple sclerosis in uncle and nephew have been described by Reynolds (1904) and by Curschman (1920).

In many cases some nervous defect, such as weakness of gait, tremors, paralysis agitans and progressive paralysis has been described in one of the parents of the patient.

But the commonest condition of recurrence of the disease in the family is that of two or more affected persons in the same fraternity (Figs. 3 and 4).

In conclusion, I venture the suggestion that whatever may eventually prove to be the endogenous cause of multiple sclerosis, the factor of heredity cannot be left out of consideration. Just as tumors inoculated into a mouse will or will not grow, according to the racial constitution of the mouse; and just as *Bacillus tuberculosis* that inhabits the body of all of us does or does not flourish there, depending on the constitution and condition of the person, so probably there are internal conditions that inhibit and others that facilitate the development of this disease or the endogenous factors on which it depends. Therefore the manifestations or symptoms of the disease vary in different persons, and they are sometimes very similar in closely related people because the hereditary factors of the constitution in which they operate are similar.

It seems most probable that the geographic, ethnologic and familial distributions shown by multiple sclerosis depend in part on one or more hereditary factors.

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STATISTICS OF MULTIPLE SCLEROSIS*

INCLUDING A STUDY OF THE INFANTILE, CONGENITAL, FAMILIAL AND HEREDITARY FORMS AND THE MENTAL AND PSYCHIC SYMPTOMS

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This study is based on the records of 1,970 cases of multiple sclerosis. Of the total, 1,773 represent cases culled from literature and 197 those whose records I have personally studied. Of the latter, fifty-five are from the Vanderbilt Clinic, ninety-three from the Mount Sinai Hospital and forty-nine from the Montefiore Hospital.

The object of the investigation was to determine the comparative incidence of the disease in the United States and Europe, the ages (including the ages of onset), average duration, sex, civil status, occupation and nativity. Special study was made of cases reported as hereditary, congenital, familial and infantile. Although the matter of personality (psychic and mental manifestations) does not come within the purview of a statistical study, attention was paid to this aspect of the symptomatology of the disease.

With the exception of a few recent reports in the literature, most of the statistical records date back many years, especially those which have appeared in this country. The diagnosis of multiple sclerosis was more rigidly dependent on the Charcot triad in the earlier days and many reports date back to the time when the Babinski phenomenon was unknown and when the significance of absent abdominals in multiple sclerosis was not appreciated. The more elastic conception of the disease on the part of European (more especially German) neurologists may account for some of the differences in the reported comparative incidence of the disease. It may be said, too, that critical study of case reports frequently leads one to doubt the diagnosis. This is especially true of cases recorded as infantile, congenital, hereditary and familial. I have therefore taken special pains to study, as far as was possible, the histories of many of the cases of multiple sclerosis recorded in the literature, which bore on statistics, especially those of the last mentioned group. I reviewed each of the 197 records of the cases which make up my own study. Another point of importance

* Read before the Association for Research in Nervous and Mental Diseases, New York, December, 1921.

is that, with very few exceptions, all the diagnoses of multiple sclerosis are made on clinical and not on pathologic grounds.

Discrepancies occur in the various totals because the statistics recorded in the literature are not uniform. Some investigators merely refer to the percentage incidence, others speak only of sex, still others only of ages or duration. American records are especially meager, and with the exception of Jeliffe's,[1] rather incomplete. This makes comparison between American and European statistics somewhat uneven; nevertheless, there is a sufficient number of records for a fairly satisfactory comparison. Perhaps it should be pointed out that the continental statistics cover practically the whole of Europe, whereas the

TABLE 1.—NUMBER OF CASES IN THE UNITED STATES

Jeliffe	109	Frankel	18	
Hammond	47	Sachs	15	
Collins	46	Taylor	9	
Stieglitz	34	Fisher	8	
Starr	27	Onuf	8	
Total			321	
Mount Sinai Hospital (1912-1920)			93	
Montefiore Hospital (1914-1921)			49	
Vanderbilt Clinic (1918-1920 and half of 1921)			55	
				518
NUMBER OF CASES IN EUROPE				
Berger	207	Lent	51	
Klausner	126	Lotsch	45	
Bramwell	100	Mauschner	40	
Kraft-Ebbing	100	Berlin	39	
Hoffman*	100	Birley and Dudgeon	35	
Uhtoff	100	Morawitz	33	
Gaehlinger	86	Blumreich and Jacob	29	
Müller	75	Nolda	26	
Bruns	70	Redlich	23	
Jolly	59	Marburg	22	
Schupfer	59	Sanger	17	
				1,452
Total number of cases of multiple sclerosis				1,970

* Hoffman, J.: Die multiple Sklerose des Centralnervensystems, Deutsch. Ztschr. f. Nervenh. **21**:1, 1901-1902.

American statistics, if not limited to New York City, embrace only a small part of the country. Some of the totals recorded by European observers, especially in the infantile group, embrace a number of cases which have been included by other compilers in their study of statistics. By referring to the originals and by cross references I have tried to avoid recording the cases more than once.

TOTAL NUMBER OF CASES

Of the 1,970 cases recorded, 518 are from America and 1,452 from Europe. Deducting the 197 cases personally studied there remain 321 American cases whose records date back many years, none being more

1. Jeliffe, S. E.: Multiple Sclerosis: Its Occurrence and Etiology, J. Nerv. & Ment. Dis. **31**:446 (July) 1904.

recent than 1903. Most of the European statistics are not any more recent, but they are spread over a greater number of years.

INCIDENCE

In America multiple sclerosis used to be looked on as a rare disease. Recent records prove that it is not so uncommon in this country as was formerly believed. Morawitz [2] states that it is the most common organic nervous disease in rural populations and gives the following figures: multiple sclerosis thirty-three cases, tabes twenty and cerebrospinal syphilis ten. Cassirer [3] says that next to tabes and syphilis of the nervous system multiple sclerosis is the most common disease. Müller [4] also speaks of it as the most common organic disease. Neither gives figures. These statements are not quite borne out by my records. While there were forty-nine cases of multiple sclerosis in the Montefiore Hospital between 1914 and 1921, there were 167 cases of syphilis of the nervous system divided as follows: tabes eighty-five, general paresis seventeen and cerebrospinal syphilis sixty-five. In the Mount Sinai Hospital there were 562 cases of syphilis of the nervous system to ninety-three of multiple sclerosis, almost 6 to 1, divided thus: tabes 160, general paresis eighty-five and cerebrospinal syphilis 317. It should be explained that the Mount Sinai figures are not statistically conclusive for the reason that during the period covered special study of syphilis of the nervous system was carried on and effort was made to admit an unusual number of cases.

The highest percentage recorded in Europe is that by Mauschner [5] in the Tubingen Clinic, that is, 2.5. The lowest by Jolly (Berlin) as 0.84. Williams of England gives a percentage of 2.2. The highest of the older American statistics is that of Frankel, 1.7 and the lowest by Taylor [6] 0.09, even if we include his doubtful cases.[7] Frankel's figures were high because they represented the incidence among organic cases only. The recent Montefiore Hospital records (1914-1921) show a percentage incidence of 4.3 while the recent Mount Sinai Hospital records (1912-1920) give 2.9 per cent. Both these figures, repre-

2. Morawitz, P.: Zur Kenntness der multiplen Sklerose, Deutsch. Arch. f. klin. Med. **82**:151, 1904-1905.

3. Cassirer, R.: Ueber eine besondere Lokalisations—und Verlaufsform der multiplen Sklerose, Monatsch. f. Psychiat. u. Neurol. **17**:193, 1905. Die multiple Sklerose in Wichtigsten Nervenkrankheiten in Einzeldarstellung, Leipzig, 1915.

4. Müller, Eduard: Die multiple Sklerose des Gehirns und Ruckenmarks, Jena, 1904.

5. Mauschner, Ernest: Multiple Sklerose und Unfall, Arch. f. Psychiat. **3**: 1917.

6. Taylor, E. W., and Meyer, J. W.: Boston M. & S. J. **148**:393, 1903.

7. Unless otherwise mentioned, the percentages stated refer to the total number of cases both organic and functional.

senting ward (organic) cases, are lower than Bramwell's,[8] which are 5.5 per cent. for all ward cases (also presumably only organic). Bramwell's figures for all clinic patients are 1.7 per cent.

Computing all the European records together we get an average incidence of 1.33 per cent., while all the old American records gave only 0.36 per cent. These figures may be compared with what Bramwell found in 1903, that is 1:82, or 1.2 per cent., in Europe, and 1:219, or 0.46 per cent, in the United States. The recent American figures

TABLE 2.—Percentage of Incidence in the United States

	Old Records		Percentage
Jeuffe	109 cases out of	31,502	0.34
Hammond	47	10,000	0.47
Collins	46	9,508	0.5
Starr	27	10,056	0.27
Frankel	18	1,050	1.7
Taylor	9	9,783	0.09
Fisher	8	2,451	0.32
Onuf	8	500	1.6
Total	272	74,850	0.36
	Recent Records		**Percentage**
Mount Sinai Hospital	69 cases out of	2,359	2.9
Montefiore Hospital	49	1,144	4.3
Vanderbilt Clinic	55	11,859	0.46
Total	173	15,362	1.1

TABLE 3.—Percentage of Incidence in Europe

			Percentage
Bruns (Hanover)	70 cases out of	5,500	1.33
Bramwell (England)	100	5,825	1.7
Jolly (Berlin)	59	6,979	0.84
Mauschner (Tubingen)	40	1,602	2.5
Saenger (Hamburg)	17	1,684	1.0
Total	286	21,590	1.33

show a percentage of 1.1 of all cases, which is three times the old ones, and almost approaches the European. Combining the Mount Sinai and Montefiore records,[9] 2.9 per cent. and 4.3 per cent., respectively, we

8. Bramwell, Byrom: The Prognosis of Disseminated Sclerosis, Rev. Neurol. & Psychiat. **3**:161, 1905; Relative Frequency of Disseminated Sclerosis in Scotland and North of England and in America, ibid. **1**:12, 1903.

9. It will be noticed that the Mount Sinai Hospital percentage is computed on a total of sixty-nine cases out of 2,359, whereas the total number of histories of multiple sclerosis numbered ninety-three. This is because the diagnosis was doubtful in twenty-four cases, and I included only those in which it was absolutely certain clinically. The same applies to the Montefiore Hospital records; only of this group I excluded, besides doubtful cases, also records of patients who had previously been at the Mount Sinai Hospital. Had I included the latter, and for the purpose of computing the statistics of the Montefiore Hospital alone there is reason for doing so, the percentage incidence of that institution would have been considerably higher.

get a percentage of 3.36 for organic cases. It will be seen, therefore, that the average incidence of multiple sclerosis in this country has risen considerably during the last twenty years; but whether due to more accurate diagnosis or extension of the disease concept or to actual numerical increase cannot be stated from the figures alone.

AGE

Multiple sclerosis occurs in all ages, from early childhood to very old age. It has been described in about 100 cases in children. (This will be discussed fully when we come to consider the infantile, congenital, familial and hereditary forms.) In the literature mention is made of patients as young as 1½ and 3 and 4 years. The youngest

TABLE 4.—AGES OF PATIENTS WITH MULTIPLE SCLEROSIS

Combined Vanderbilt Clinic, Montefiore and Mount Sinai Hospitals			Klausner		Marburg		Müller	
Age	Number	Percentage	Age	Number	Age	Number	Age	Number
Below 10	1	0.5	0- 5	2	10-20	4	15-20	12
11-20	11	5.7	6-10	2	21-30	9	21-30	33
21-30	65	33.5	11-20	17	31-40	6	31-40	23
31-40	72	37.0	21-30	38	41-50	1	41-50	6
41-50	36	18.5	31-40	36	51-60	1	51-60	1
51-60	8	4.1	41-50	17				
61-65	1	0.5	51-60	7				
			61-65	2				
	194			121		71		75

Berger		Jeliffe		Morawitz		Borst (from Literature)	
Age	Number	Age	Number	Age	Number	Age	Number
0- 8	8	0-10	9	0-10	1	1- 5	5
10-20	49	10-20	8	10-20	16	6-10	10
20-30	83	20-30	21	20-30	14	11-20	45
30-40	51	30-40	27	30-40	10	21-40	306=70%
40-50	10	40-50	20	40-50	2	41-50	41
50-60	5	50-60	19			51-60	29
						61-65	2
	206		104		43		438

recorded by myself was 10 years, with the onset of the illness at 7. Crocq (quoted by Jeliffe) speaks of a patient of 81 years, but in all other records no mention is made of patients above 65. The disease is most common between the ages of 20 and 40, about 70 to 75 per cent. of all cases. Cassirer thinks it is most common in the third decade. Of a total of 428 cases collected by Borst,[10] 306, or 70 per cent., were between 20 and 40. Birley and Dudgeon[11] give the average age as 28.6 years. Jeliffe records an unusually large number between 50 and 60—18 per cent. Table 4 may serve for comparison.

10. Borst, Max: Die multiple Sklerose des Zentralnervensystems, in Lubarsch u. Ostertag: Ergebnisse der algemeinen Pathologie **9**:66, 1903-1904.

11. Birley, J. L., and Dudgeon, L. S.: Clinical and Experimental Contribution to the Pathogenesis of Disseminated Sclerosis, Brain **44**:150, 1921.

DURATION

Two different notions are implied under the term duration. One refers to the length of the period from the onset of the first symptom to the time the patient comes under observation, the other is the total duration from the onset of the illness to death. The first, assuming it is always possible to tell the time of onset of the first symptom, is somewhat easier to estimate than the second, because most patients are not followed to the very end. Indeed nearly all the records refer to the first notion of duration. It is important to bear in mind these two different notions in the bearing they have on prognosis, because it is obvious that the same patient the duration of whose illness under the first concept is estimated, say, at six months, may still be alive twenty years hence, and in a subsequent study be classed under the second notion of duration.

TABLE 5.—DURATION OF ILLNESS

	Combined Vanderbilt Clinic, Montefiore and Mount Sinai Hospitals	Bramwell		
Less than 6 months	31	Fatal Cases:		
7 months to 1 year	15	1- 4 years	10	
13 months to 2 years	47	5- 9 years	13	
2- 3 years	27	10-14 years	8	
3- 4 years	11	15-21 years	4	
4- 5 years	15			35
5- 6 years	7	Alive—Worse		33
7-10 years	28	Unimproved		16
11-15 years	9	Improved		8
16-20 years	1	Well		4
21-25 years	1	Unknown		14
	192			110

Birley and Dudgeon give the average duration from the onset of the illness to the time of examination as four years, the shortest being three weeks and the longest fourteen years. Marburg [12] gives the duration in twenty-two cases he studied as from twenty-six days to thirteen months, one exception being three years. Bramwell gives the average duration in thirty-five fatal cases as seven years and nine months—(seven months to twenty-one years). He records the longest duration in a living patient as thirty-three years, and six cases between twenty and thirty years. My own records show one patient with a history of twenty-five years' duration. Five of my patients gave a history of one month or less. Comparative tables are given in the following.

12. Marburg, Otto: Die sogenannte akute multiple Sklerose (Encephalomyelitis periaxialis scleroticans), Jahrb. f. Psychiat. u. Neurol. **27**:211, 1906.

SEX

The male sex is more often affected than the female, in the ratio of nearly three to two. Of twenty-six records only six speak of greater incidence among females, the latter being those of Charcot, Berlin, Müller, Bruns [13] and Stelting, Morawitz and Birley and Dudgeon.

TABLE 6.—SEX OF PATIENTS WITH MULTIPLE SCLEROSIS

	Europe					United States		
	Male	Female		Male	Female		Male	Female
Berger	140	66	Berlin	13	26	Jelliffe	68	41
Klausner	78	44	Morawitz	15	18	Stieglitz	17	17
Kraft-Ebbing	58	42	Charcot	9	25	Sachs	10	5
Uhtoff	67	33	Birley & Dudgeon	12	22	Moran	4	4
Müller	35	40	Blumreich & Jacob	23	6	Montefiore Hosp.	26	23
Hoffman	53	47	Nolda	16	10	Vanderbilt Clinic	36	19
Probst	34	24	Redlich	12	11	Mount Sinai Hosp.	55	38
Bruns & Stelting	13	25	Marburg	11	11			
Lent	37	14	Cassirer	2	4			
Lotsch	30	15						
				658	484		216	147
				or	or		or	or
				58%	42%		57%	43%

	Male		Female	
	Number	Per Cent.	Number	Per Cent.
European cases	658	58	484	42
United States cases	216	57	147	43
Total cases	874	58	631	42

These figures represent about 15 per cent. of the total number of cases reviewed. The American and European statistics very nearly coincide in this respect.

OCCUPATION

Morawitz states that multiple sclerosis is most common in the rural (agricultural?) population. It is said to affect mainly the laboring class. My own statistics do not confirm either view, though it is hardly fair to contradict the first statement since all of my patients come from

TABLE 7.—OCCUPATION OF PATIENTS

Soldier	Pressman	Candymaker	Newsdealer
Cashier	Salesman	Student	Domestic
Teacher	Carpenter	Storekeeper	Bellboy
Machinist	Houseworker	Weaver	Artist
Tailor	Roofer	Printer	Chauffeur
Pedler	Cook	Baker	Iron worker
Laborer	Clerk	Cigarmaker	Policeman
Painter	Driver	Bartender	
Cutter	Butcher		

New York City. Practically every occupation is represented in my list of cases, as shown in Table 7. Obviously all general ward patients come from the working people.

13. Bruns, L.: Ueber die Erkrankungen der Sehnerven im Frühstadium der multiplen Sklerose, Neurol. Zentralbl. **18**:475, 1899.

NATIVITY

The following figures are practically limited to New York City, and it is obviously not altogether true to speak of them as representative of the whole United States. There are more than four times as many cases among those of foreign birth as among natives. Even allowing for the great number of foreign born in New York—and they constitute roughly only two fifths of the population—it is difficult to account for the unusual excess of foreigners over natives. The fact in itself, however, may possibly account for the greater incidence of multiple sclerosis in Europe as compared to America, although in his study covering fifteen years (1888-1903) Jeliffe gives more nearly even figures: Forty-seven native and fifty-four foreign born. The following table refers to my own cases.

TABLE 8.—NATIVITY OF PATIENTS WITH MULTIPLE SCLEROSIS

	Native		Foreign Born	
	Number	Per Cent.	Number	Per Cent.
Mount Sinai Hospital	11	11.8	82	88.2
Montefiore Hospital	6	12.2	43	87.8
Vanderbilt Clinic	19	34.5	36	65.5
Total	36	18.3	161	81.7

CIVIL STATUS

Multiple sclerosis is more common among married people than among single ones, but this fact is accounted for by the greater incidence of the disease during the ages between 20 and 50. The fact, therefore, cannot be said to have special significance. Except my own, there are no statistics bearing on this point.

TABLE 9.—CIVIL STATUS

	Married		Single	
	Number	Per Cent.	Number	Per Cent.
Mount Sinai Hospital	60	64.5	33	35.5
Montefiore Hospital	23	60.5	15	39.5
Vanderbilt Clinic	35	63.6	20	36.4
Total	118	63.5	68	36.5

MULTIPLE SCLEROSIS IN CHILDREN

Opinions vary as to the existence of multiple sclerosis in children. In alluding to four cases of early multiple sclerosis which he had seen (4, 7, 12 and 13 years, respectively) Oppenheim [14] expressed the opinion, in 1887, that "the beginning of multiple sclerosis in adults

14. Oppenheim, H.: Zur Pathologie der disseminierten Sklerose, Berl. klin. Wchnschr. **24**:904 (Nov. 28) 1887.

cannot infrequently be traced to the very earliest childhood." Müller states that "proof of the existence of infantile multiple sclerosis is still missing, but it may trace its beginning to childhood" and "the development of the process on the basis of a congenital predisposition (is) most likely." It may be pointed out that congenital predisposition is a vague expression, capable of numerous interpretations.

One of the early, exhaustive studies of infantile multiple sclerosis was made by Schupfer.[15] He studied fifty-eight cases recorded in the literature up to 1902 and included one case of his own. This was in a child of 11, who at 9 had an acute illness with fever, coma, convulsions, paralysis and ocular palsies. Although Schupfer includes this case in his group of multiple sclerosis, it is obvious from the history, no matter what the clinical findings were at the time of the examination, that he was dealing with a case whose inception corresponds to a meningitis or meningo-encephalitis. Most of the cases he records are neither clinically nor pathologically multiple sclerosis. Congenital syphilis would account for many of them. Hereditary spinal spastic paralysis, Friedreich's ataxia, hereditary cerebellar ataxia, encephalitis, tumors of the brain, cerebral palsies of children, the Little and Foerster types, all these are represented in the group recorded by Schupfer. Nevertheless, it must not be inferred that this author has not critically analyzed his material; he would still include twenty-eight of the fifty-nine cases as true instances of multiple sclerosis in children.

In 1909 Gaehlinger[16] reviewed the histories of eighty-six cases of multiple sclerosis out of a total of ninety-one reported as having occurred in children below 15, some even in infancy. All the cases were taken from the literature and included those recorded by Schupfer (1902) and Baboneix (1904). Gaehlinger concluded that "none of the observations have given us absolute proof of the existence of infantile multiple sclerosis." This despite Oppenheim's ingenious theory that all multiple sclerosis begins in infancy and only manifests itself later in life. Gaehlinger also emphasizes the difficulty of diagnosis. To which may be added the unreliability of most histories, the unusual difficulty in tracing the onset of the earilest symptoms and the inability to exclude fever or infectious diseases as etiologic factors. The same author also mentions Friedreich's ataxia, chorea, Little's disease, cerebral sclerosis, family spastic paraplegia, tumors of the brain, disseminated syphilis (congenital), hysteria and encephalomyelitis, as more likely diagnoses. The recent epidemic of encephalitis justifies the addition of this disease as a likely possibility.

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15. Schupfer, F.: Ueber die infantile Herdsklerose, Monatschr. f. Psychiat. u. Neurol. **12**:61 and 89, 1902.

16. Gaehlinger, M. H.: Contribution à l'étude de la sclérose en plaque infantile, L'Echo méd. du Nord. **13**:37 (Jan.) 1909.

Eichhorst [17] reviewed the literature up to 1896. He mentioned the fourteen cases recorded by Marie up to 1883, the nineteen by Unger up to 1887 and those by Nolda [18] up to 1891. Eichhorst added a case of his own, that of a boy of 8. (His mother had multiple sclerosis, as was shown at necropsy.) The boy also died and came to necropsy. Microscopic section of the boy's cord showed multiple sclerosis. Of the other twenty-six patients only three came to necropsy. In those three instances the cord was not examined, and the reports show that other brain changes besides sclerosis were found. Nolda's case was that of a boy of 9 whose disease began at 7 and whose clinical picture was typical of multiple sclerosis. Weisenburg [19] reported the cases of a girl of 4 and a boy of 15—brother and sister.

Armand-Delille [20] described a case of multiple sclerosis in a child of 5. Raymond and Beaudouin [21] reported the case of a girl of 13 whose symptoms began at 10. Neither is conclusive. Raymond and Lejonne [22] speak of a girl of 9 years whose condition was progressive and whose signs and symptoms were apparently those of multiple sclerosis. But the history was that of a disease with an acute onset which lasted three weeks, and leaves the question of meningitis unanswered. Stieglitz [23] records three cases in which the patients were 9, 11 and 15, respectively. All three are doubtful from the description of the clinical picture; but in fairness it must be said that the diagnosis of multiple sclerosis was definite in that author's mind.

Schuler, mentioned by Nolda, reported a case of multiple sclerosis in a child, which was proved by necropsy. Rauschburg,[24], 1909, reported the case of a boy of 7 who had partial paraplegia, intention tremor and slight speech disturbance. The disease began at 1½ years of age; there was no history of previous illness and no hereditary factor. Although the case is not proved pathologically, the diagnosis seems not

17. Eichhorst, Herman: Ueber infantile u. hereditare multiple Sklerose, Virchows Arch. f. path. Anat. **146**:173, 1896.

18. Nolda, August: Ein Fall von multipler Hirn—und Ruckenmarksklerose im Kindesalter, Arch. f. Psychiat. **23**:565, 1891-1892.

19. Weisenburg, T. H.: Multiple Sclerosis. Its Occurrence in a Family, Arch. Diagnosis **2**:167 (April) 1909.

20. Armand-Delille, M. P.: Symptoms de sclérose en plaques chez un enfant de cinq ans et demi, Rev. neurol. **13**:243, 1905.

21. Raymond and Beaudouin: Sclérose enplaque infantile, Rev. neurol. **13**: 647, 1905.

22. Raymond and Lejonne: Encephalomyelite consecutive a un etat meningé chez une fillette de 9 ans, Sclérose en Plaque? Rev. neurol. **17**:367, 1909.

23. Stieglitz, L.: Multiple Sclerosis in Children, with a Report of Three Cases, J. Nerv. & Ment. Dis. **24**:174, 1897.

24. Rauschburg, P.: Ein kindischer Fall von Sklerosis multiplex, Neurol. Centralbl. **28**:622, 1909.

improbable. Schlesinger,[25] 1909, described the case of a boy whose history, signs and symptoms pointed to a subacute process. The diagnosis of disseminated sclerosis was made because of the multiplicity of symptoms and the eye signs (optic atrophy). Encephalomyelitis was considered as a possible cause. The patient died and came to necropsy. Macroscopic and mircoscopic study confirmed the diagnosis of subacute multiple sclerosis.

In my record from the Mount Sinai Hospital there is the history of a boy of 10 who was normal up to the age of 6½ when he developed sudden paralysis of the right arm and later of both legs. There was no fever, headache, vomiting or other symptoms of acute illness. Abdominal reflexes were absent; there was a left Babinski sign and normal electrical reactions. He recovered from this attack and within the next three years had four others in which he had ataxia, tremor, the Babinski sign and laughing spells, and the abdominal reflexes were absent. Fairly good recovery followed each attack. The remissions, together with the signs and symptoms, seemed to justify the diagnosis of multiple sclerosis. In the Montefiore Hospital records there is the history of a girl of 18 whose illhess began at the age of 8 with difficulty in walking, weakness of the hands, incontinence of urine. Physical examination revealed a spastic gait, tremor of both hands, lively deep reflexes, bilateral clonus, a Babinski sign and the absence of abdominal reflexes. Clinically there seems to have been no question as to the diagnosis of multiple sclerosis. Another case is that of a young woman of 27, the onset of whose illness dates back definitely to the age of 13. Physical examination revealed nystagmus, intention tremor, absence of abdominal reflexes, bilateral Babinski sign and pallor of the optic disks.[26]

There are eight other cases in my records which began, respectively, at 14, 15, 16 and 17 years. The histories of three of these are not reliable, and the diagnoses are doubtful. There remain five cases, one in a patient of 14, two of 16 and two of 17, in whom the clinical diagnosis of multiple sclerosis was not to be questioned. As the period of childhood cannot be stretched beyond 15 years, there remains only one other case of 14 which may be included in the group of early multiple sclerosis. We have, then, four cases occurring in a total of 197 children, or 2 per cent.

From this study one may draw a fairly definite conclusion as to the existence of multiple sclerosis in children. The vast majority of

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25. Schlesinger, Hermann: Zur Frage der akuten multiplen Sklerose und der Encephalomyelitis disseminata im Kindesalter. Arbeiten aus dem Neurologischen Institut. Wien. **17**:410, 1908-1909.

26. These cases will be reported at greater length in a special paper on "Multiple Sclerosis in Children."

cases stand unproved. In those instances the diagnoses were erroneous; yet it is difficult to explain why careful observers should have attempted to prove the existence of infantile multiple sclerosis by means of doubtful cases. Those were very likely atypical, but could be better explained by the diagnosis of congenital disseminated syphilis, various traumatic birth palsies, spastic diplegias, Little's or Foerster's types of disease, family spastic paralysis, Friedreich's disease, tumors of the brain, hysteria, encephalomyelitis and cerebral sclerosis. Nevertheless, a few authentic cases remain. These have been proved, both clinically and pathologically, to have been multiple sclerosis. Its existence, therefore, in children, while rare and in need of scrutiny, cannot be doubted.

FAMILIAL, CONGENITAL AND HEREDITARY MULTIPLE SCLEROSIS

The question of familial, congenital and hereditary influence in disease in general and multiple sclerosis in particular is in need of strict definition. Loose interpretation of the meaning of those terms is responsible for many broad and erroneous conclusions. To speak of a congenital or hereditary predisposition, while possibly permissible, is not very meaningful. In order that a disease be considered congenital one must prove its existence in the parent at the time of or subsequent to inpregnation, that it was transmitted to the germ plasm or embryo or fetus in utero and that it was present in the child at birth, although it need not have manifested itself immediately afterward. So, too, to speak of heredity one must show that the disease existed in some of the ascendants and collaterals, that it manifested itself in the descendants and that it affected the various persons with a fair degree of consistency or regularity. True mendelism will not accept, of course, an interpretation of heredity which does not conform to its laws. Further, one isolated instance cannot be accepted as proof of a general conclusion because there are too many possibilities by the law of chance, among so many hundreds and thousands of cases, that the disease may appear hereditary. The same may be said, although with less emphasis, about familial influence in disease.

There are, moreover, two distinct notions of hereditary or familial influence in nervous diseases which are current in medical literature. The older, which is gradually being discarded, is to consider any nervous disease in the family as a possible influence on or cause of any other nervous disease. Thus it is not unusual to find epilepsy, alcoholism, insanity, hysteria, neurasthenia, fright and exhaustion mentioned as possible hereditary (!) causes of multiple sclerosis. The more recent view, of course, and perhaps sounder, is to accept only the given disease in the consideration of familial, hereditary and congenital factors.

Whether or not these factors operate in multiple sclerosis cannot be definitely answered, but there are numerous instances in which the disease occurred in parent and offspring. Among my own records there is one instance in nearly 200 cases; it is that of a woman of 55 who had multiple sclerosis, which began at 50, whose son died from the same disease at 22. This instance cannot be looked on as congenital as the mother developed the disease twenty years after the birth of her son.

Eichhorst cites a case in which there may have been a congenital factor. A woman who had typical multiple sclerosis for two years gave birth to a child who developed the disease. The mother died at 42 and the child at 9. Necropsy showed a typical sclerosis of the cord. Two children born before their mother had the disease did not have it. Pelizaüs [27] reports an hereditary disease which occurred in three generations of males and was transmitted through the mother. It showed itself in one son, three grandsons and one great grandson. Pelizaüs believes that the disease was multiple sclerosis. The clinical picture was the same in all cases and came on at the same ages in all. There was bilateral nystagmus, speech disturbances, spastic paraplegia without atrophy, increased reflexes, intact sensibility and moderate dementia. Although persual of the clinical histories does not altogether convince one, Pelizaüs seems to be of the opinion that all were cases of multiple sclerosis.

Klausner [28] reports two cases in a brother and sister of 25 and 27 years, respectively. Weisenburg reports two cases in a brother and sister, whom he personally observed, and a third member of the same family who is said to have suffered from the disease. The brother developed the disease at 15 and the sister at 4. The family was English. Reynolds [29] reports three cases, the second, fourth and sixth in one family, a sister and two brothers of 33, 30 and 27 years, respectively. The parents were psychopathic. He further quotes another English family in whom the first and third developed multiple sclerosis at 25 and 15 years, respectively. Frerichs and Erb (quoted by Borst) mention the disease in siblings, Totzke in two sisters of 11 and 14 years and Elta in mother and son. Among the records of the Montefiore Hospital are found two instances in which the disease occurred in brother and sister.

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27. Pelizaüs, F.: Ueber eine eigentümliche Form spastischer Lähmung mit cerebralerscheinungen auf hereditärer Grundlage, Arch. f. Psychiat. **16**:1885.

28. Klausner, Irma: Ein Beitrag zur Aetiologie der multiplen Sklerose, Arch. f. Psychiat. **34**:841, 1901.

29. Reynolds, E. S.: Some Cases of Family Disseminated Sclerosis, Brain **27**:1904.

Merzbacher [30] reports the case of a family with eleven members in whom a disease very much like multpile sclerosis developed in the fourth month of the lives of the persons. The patients had nystagmus and tremor of the head. One came to necropsy at the age of 20 and on microscopic examination the myelin sheaths were found totally absent. No extensive description is given. Coriat [31] reports a peculiar form of family nervous disease resembling multiple sclerosis occurring in children. There were four patients of Russian Hebrew parentage, two of them being a brother and sister, one a boy of 18 and one a girl of 8.

From these cases it may be seen that the evidence is not conclusive. Eichhorst's isolated instance may be looked on as possibly illustrating congenital transmission. The numerous other instances in which the disease occurred in more than one member of a family or in parent and offspring cannot be considered, in view of its comparative prevalence, as absolute proof of familial and hereditary forms of multiple sclerosis. In this connection, too, one need consider the relation of the experimental investigations as to the etiology of multiple sclerosis. This disease has come to be looked on as the result of a subacute or chronic infection, and the gliosis has been interpreted as a reaction to inflammation. Obviously it makes some difference so far as this discussion is concerned whether the inevitable focal infection plays any causative rôle or a spirochete is the etiologic factor or "abiotrophy" and "systemic degeneration" are invoked to explain the genesis of the disease. It is quite possible, however, that the discovery of the causative agent of multiple sclerosis will clear up the question of the existence of familial, hereditary and congenital types.

PSYCHIC AND MENTAL DISTURBANCES

Attention has commonly been called to the existence of psychic and, more especially, emotional disturbances in multiple sclerosis, and numerous reports of cases in which the patients showed those symptoms are to be found alike in American and European literature. Comparatively fewer statistical facts bearing on mental symptoms exist in American literature, whereas a number of European writers have reported extensively on this subject. In many cases it is not easy to draw a sharp line between mental and psychic symptoms. Oppenheim, for instance, looks on the impulsive laughter occasionally found in multiple sclerosis as a neurologic sign of thalamic involvement and not as a psychic symptom as commonly understood.

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30. Merzbacher: Eine eigenartige familiäre Erkrankung des Zentralnervensystems, Neurol. Centralbl. **26**:1139, 1907.

31. Coriat, Isador: A Peculiar Form of Family Nervous Disease Resembling Multiple Sclerosis Occurring in Children, Boston M. & S. J. **160**:506, 1909.

Under psychic symptoms are mentioned general nervousness, irritability, sleeplessness, mild depression, lack of concentration, emotional or affective disturbances. While these symptoms are commonly encountered, they cannot be said to be characteristic of multiple sclerosis. Many patients, however, show graver disturbances, and indeed to such an extent as to dominate the whole clinical picture and to lead to erroneous diagnoses. This is especially true of hysteria. More rarely hysteria simulates multiple sclerosis. Thus Parhon and Goldstein [32] mention a case of hysteria which simulated multiple sclerosis so closely that the diagnosis was made only at necropsy. Zilgien [33] reports the case of a young man of 23 who for two years had hysterical symptoms, stammering and laughter, and was ultimately proved to have multiple sclerosis. The same author also speaks of a woman of 33 who for four years, up to the time of her complete recovery, was looked on as having multiple sclerosis. Healey [34] reported a case in which the diagnosis between multiple sclerosis and hysteria was doubtful for a long time.

Mendel believes that psychic symptoms are present in all cases of multiple sclerosis and Lannois is convinced that they occur quite regularly (quoted by Raecke [35]). Berger [36] mentions nervousness as occurring in nineteen, or 9 per cent., of his cases and pronounced psychic disturbances, such as irritability, depression, memory defects in twenty-four, or 12 per cent. Incidentally he mentions three cases of epilepsy in his 206 cases. Fourteen of his patients showed irritability, eight mild depression, four euphoria and eighteen mild memory defects. Morawitz mentions memory weakness in eight of thirty-three cases.

Next to hysteria, paresis is said to occasion diagnostic difficulties. Raymond and Touchard [37] report a case of multiple sclerosis which began with symptoms simulating general paresis. The patient had epileptiform attacks, change of character, defective memory and disturbances of speech. It is well known, of course, that paresis may for a time simulate multiple sclerosis. I have even now a patient under observation whose symptoms for many months consisted of spastic

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32. Parhon and Goldstein: Un cas d'Hysterie simulant la sclérose en plaque et la syringomyelie, Rev. neurol. **13**:862, 1905.

33. Zilgien, H.: De l'importance des symptôms hystériques dans l'étude de la pathogénie et du diagnostique de la sclérose en plaque, Rev. méd. de l'Est. **37**: 673, 1905.

34. Healey, W., Jr.: J. Nerv. & Ment. Dis. **36**:164, 1909.

35. Raecke: Psychische Störungen bei der multiplen Sklerose, Arch. f. Psychiat. **41**:482, 1906.

36. Berger, Arthur: Eine Statistik über 206 Falle von multipler Sklerose, Jahrb. f. Psychiat. u. Neurol. **25**:168, 1905.

37. Raymond and Touchard: Sclérose en plaque debutant par des troubles mentaux simulant la paralysie général, Rev. neurol. **17**:224, 1909.

paraplegia, ataxia, tremor, nystagmus and scanning speech. It was only after many months that pupilary changes and mental deterioration called attention to the paretic picture. The diagnosis was confirmed by the positive Wassermann reaction in the blood and spinal fluid. Geay,[38] in speaking of psychic symptoms in multiple sclerosis, stresses the point that the disease is mostly to be differentiated from hysteria and paresis and concludes that the mental symptoms may range from simple enfeeblement of memory to complete obnubilation. Spiller and Camp [39] reported a patient (the case came to necropsy) with suicidal tendencies. Charcot early called attention to dulness, indifference, slowness to grasp things and delusions, besides memory weakness and impulsive laughter. Probst found a few patients (five out of fifty-eight) with high grade dementia.

Raecke has made an excellent study of psychic and mental symptoms in multiple sclerosis. He reviewed the literature extensively and included a review of thirty-seven cases of his own. He states that thirteen patients showed definite dementia and nine others psychic disturbances. The initial symptoms usually were depressive and maniacal, with, at times, delirial episodes. The latter were particularly to be found in patients with convulsions. Affective disturbances were common. He quotes a number of authors on the subject. Thus, Gowers spoke of rare cases of insanity based on multiple sclerosis. Redlich mentions idiocy, confusion, irritability and hallucination as being more common in multiple sclerosis than was formerly believed. Meinert speaks of general disturbances of intellect and enumerates eroticism, irritability, memory weakness, melancholia, depression, insomnia, euphoria, paranoidal delusions and suicidal trends as possible mental symptoms. Oppenheim, on the other hand, believes that high grade dementia and delusions are uncommon in multiple sclerosis. Seiffer [40] also made a comprehensive study of mental disturbances in multiple sclerosis. His conclusions are: 1. The disease may be totally free from mental symptoms. 2. The longer the duration of the disease the more likely and the more pronounced the disturbances of intelligence. 3. There is no correspondence between the intelligence defect and the educational level of the patient. 4. There is a close connection between the intelligence defect and the clinical type of the disease, patients with cerebral defects giving the most symptoms and those with spinal signs fewest or none. 5. The dementia of multiple sclerosis

38. Geay, A.: Des trouble psychique dans la sclérose en plaque, Thése de Lyon, 1904; Rev. neurol. **13**:900, 1905.

39. Spiller, W. G., and Camp, C. D.: Multiple Sclerosis with a Report of Two Additional Cases, with Necropsy, J. Nerv. & Ment. Dis., July, 1904.

40. Seiffer, W.: Ueber psychische, insbesondere Inteligenzstörungen bei multipler Sklerose, Arch. f. Psychiat. u. Nervenkrank. **15**: 1905.

cannot be strongly differentiated from other dementias though that of the former shows great liability of mood. These sudden changes are quantitatively high and stand in no relation to the degree of dementia.

In the records of my own cases little mention is made of outspoken organic mental changes. Psychic symptoms, such as irritability, depression and general nervousness, mild memory defects and emotional changes are frequently noted. Impulsive laughter and euphoria are occasionally referred to. Hysteria seems not infrequently to have been considered as an alternate diagnosis for a time. Marked dementia was rarely encountered, delusions and hallucination practically not at all. Considering that a great many of these patients had the disease for years and years and that quite a number were inmates of the Montefiore Hospital for a very long time, it is noteworthy how few showed definite mental symptoms. In none of the cases recorded was there a complete psychosis or organic dementia.[41]

41. In addition to the references given, the following may be of interest: Abrahamson, L.: Familial Multiple Sclerosis, J. Nerv. & Ment. Dis. **33**: 1906.
Batten, F. E.: Proc. Roy. Soc. **22**:35, 1908-1909.
New York Neurological Society Meeting, Feb. 4, 1902, J. Nerv. & Ment. Dis. **29**:288, 1902.
Tredgold, A. F.: Rev. Neurol & Psychiat., July, 1904.

Abstracts from Current Literature

HALLUCINOSIS AND HALLUCINATIONS. P. SCHROEDER, Monatschr. f. Psychiat. u. Neurol. **49**:189 (April) 1921.

According to Wernicke, who coined the name, hallucinosis is characterized by the following syndrome: unimpaired consciousness; normal power of thought and undisturbed orientation; intense fear; numerous auditory hallucinations, which accord with the content of the fear; finally, a decided tendency to rapid systematization and development of delusions of persecution, generally directed against definite persons. According to Bonhoeffer, the two characteristic features are: (1) auditory hallucinations clothed in words, and (2) fear. "Gedankenlaut-werden"—the thoughts becoming audible—plays an important rôle. Explanatory delusions are common, but a closed systematization is not a part of the picture.

The author reports four cases of hallucinosis of different types. In all, the most interesting symptom is that of the thoughts becoming audible. For weeks the patient in Case 3 said that every word he said he heard repeated after him. Everything he thought he heard and recognized as his own thought content. The content of what he heard was usually indifferent. The sound was that of his own voice.

The patient in Case 1 reported that at the outset every word he read was read after him. Whatever he thought he heard spoken aloud in his own dialect. In quieter periods he was conscious that they were his own thoughts which he was hearing, but often, especially when excited, it was "someone" speaking to him.

The patient in Case 4 heard partly indifferent or senseless remarks, in part connected conversations. Frequently he was conscious that they were merely a repetition of his own thoughts. What he thought he heard at the same time. What he wanted to say he heard twice.

The patient in Case 2 at first recognized what he heard as his own thought. Later, it was others who spoke and whispered to him.

There is considerable difference between the different cases and between the condition of the same patient at different times. When insight is adequate the patient recognizes the "voices" as his own thoughts; but when a clear interpretation is no longer possible, the "voices" are frequently projected into the environment and attributed to others. According to the clarity of insight we find these various stages:

1. Echo-like repetition of thoughts.
2. Perception "as if" they were spoken.
3. Projection of what is heard to others.

From expressions of the patients we learn that the phenomenon of the hearing of thoughts—the thoughts becoming audible in Wernicke's sense—has nothing to do with auditory perception. "Hearing" refers to a form of perception for which he has no better word. One hears the voices "in his own head." Another "grasps" or "appreciates" them, saying that they do not come in through the ears. Still another says that speech, thought and hearing are not sharply separated, but glide into each other imperceptibly, and the name given varies between thought, hearing and speaking, frequently qualified by

"as if." During quiet periods, this distinction is clear. Under the influence of fear and excitement the "as if" character may be lost, and the auditory hallucinations develop a living reality.

The author describes a second type of "hearing voices" best studied in certain paranoid states in the fourth and fifth decade—where they occur in patients who are mentally clear and easy to study. These are patients who always say they are suspected—are being discussed, are being accused. They are always hearing envious words, secret whispers, sarcastic sayings. These things are not said to them, but they know it concerns them. The voices often come from a distance or through the ceiling, etc.

Unlike the "audible thoughts" these auditory hallucinations are not formulated in words. They represent the content of the anxiety or fear which is bothering the patient. The elementary factor is not thoughts become audible but an anxious delusion of reference.

The acoustic sense deceptions of the patients with hallucinosis are not as a rule true hallucinations in the textbook sense; they lack actuality; they are not equivalent for the patient to actual perception. It is only under certain conditions (excitement and fear) that they acquire reality. Generally they belong to the group of pseudohallucinations.

The author discusses at some length this distinction between hallucination and pseudohallucination. We continue to use the term hallucination in its original connotation, as defined by Esquirol—a definition which stresses the perceptual side. "An individual who has a firm conviction of a true sensation, when there is no external object in the surroundings to give rise to the sensation, such an individual has hallucinations." In the mass of cases this does not hold; the patient does not accept his hallucinations as true perception; he recognizes the distinction, and so the great majority of what we call hallucinations are really pseudohallucinations. We should cease to begin our definition of hallucinations with the usual "Hallucinations are sensations," etc. Clinical experience teaches that hallucinations are varied conscious processes in which doubts or confusions arise as to the justification for projection externally. They are not sharply demarcated from other psychopathologic phenomena in patients and not sharply separated from all processes in the normal person.

To the latter belong dreams, waking dreams, etc. The comparison of hallucinations with dreams is old, and the study of dreams will help our study of hallucinations.

Normally we have a constant activity of consciousness. This drops low at times and in deepest unconsciousness is practically nil. It is greatly influenced by external stimuli and the emotions and impulses to which they give rise, but continues to flow in the absence of such stimuli. In sleep, with its dreams, sense stimuli are absent, or almost absent. In dreams ideas have for the dreamer the full value of perception, in the absence of any sense perception. Thus to appreciate anything as real, at least under certain conditions of consciousness, adequate sense stimuli, any sense stimuli in fact, are unnecessary. If the dream material remains for a time in consciousness, it is corrected, chiefly on the basis that it does not fit into our other experiences—is in contradiction to them; according to the same standard, the cured psychotic patient corrects his psychotic experiences.

Psychologically, closely related to the dream is the delirium. Conscious processes of the value of perception without adequate stimuli characterize it as well as the dream. In content it has the same jumpiness (Sprunghaftig-

keit) and the same lack of critique, with lowered attention. The delirious patient differs from the dreamer in that he does not sleep, in that he moves and accompanies his experiences with gesture or reacts to them with actions. Hallucinations are actualities for the delirious patient, and the hallucinations of delirious patients are most real of all hallucinations. They differ so in this regard that we may consider them a third type of hallucination [(1) hallucinosis, (2) hallucination in the anxious delusion of reference, (3) delirium].

SELLING, Portland, Ore.

TORTICOLLIS AND TORSION SPASM. R. CASSIRER, Klin. Wchnschr. **6**:53 (Jan. 8) 1922.

The chapter on torticollis belongs to the "Schmerzenskindern" of neurology. The objective picture presents both an organic and a functional coloring which at times makes a differentiation impossible, and many observers continue to consider all these affections functional.

The author states that it is difficult to demonstrate any lesion of the nervous system to account for the clinical picture. Strümpell suggested a striate syndrome for torticollis resulting in abnormal tonus, spasms, movement anomalies, slowing of motion and even tremor.

In torsion spasm, which the author discusses under the heading of torticollis, there are no signs of pyramidal lesion, and one may speak of an extrapyramidal disturbance. Sensory changes do not occur. The right to speak of a striate syndrome is based on the work of Wilson, and on the works of Vogt, who, under this heading, consider a group of diseases whose likeness rests on the characteristic movement disturbances. The major portion of our knowledge in these conditions is expressed by using the term extrapyramidal movement disturbances. In two cases of torticollis observed by the author the possibility of a striate syndrome presented itself.

CASE 1.—This patient, now 58 years of age, was first examined by Oppenheim, who diagnosed the case as torticollis. Following an operation by Krause he experienced little relief, but after a year his head again became straight. This slow improvement has been noted previously in operations for torticollis. Four years after the operation the patient again noticed difficulty in muscular movements, especially in the right hand and arm. In 1913, Oppenheim advised a partial section of nerves, but because of the war the patient did not have this done. In 1920, because of the progression of the disturbance, the patient's triceps tendon was lengthened, making it again possible for him to write. After a lapse of three months the symptoms recurred with marked hyperextension of the limb and some muscle cramps in the right leg. The examination by the author at this stage of the process revealed a paralysis of the left trapezius and sternocleido mastoid. The right trapezius tendon was cut, the head was bent forward and in the right shoulder muscles there was considerable spasm. The right arm was pressed tightly against the chest, the forearm pronated and the hand held in a flexion cramp. Voluntary movements would bring on this hyperextension, and all purposeful movements were markedly impaired. The muscles of the back also showed alternating spasms so that the buttock would be pulled to the right and at times pulled about the sagittal axis. In walking the right foot had a tendency to be supinated. There were no pyramidal signs; sensation was intact and cerebral functions were unaffected. On June 6, 1921, Krause performed tenotomies and nerve sections with apparently satisfactory results.

In this case, then, there first appeared a left-sided torticollis. Later the right side became involved, and gradually there was an extension involving the entire musculature. In the literature progressions of torticollis are rarely mentioned. Lucas described a case in which the spasm involved the buttock and caused a deformity of the lumbar region. Dercum also described a similar case.

The second patient was a man, aged 29 years, who was first examined by Oppenheim in 1890. He was well up to the age of 7. At that time a change in gait was noted. He walked with his left foot turned in. When examined at the age of 12 both feet were held in adduction. The toes were dragging on the ground, and the right knee had a tendency to flexion. No diagnosis was made at that time. He was treated from a psychic standpoint without any result. The condition gradually progressed and several operations were performed without success. When examined by Cassirer the head was pulled back almost continuously. Short periods of relaxation would occur, but it was only with the greatest difficulty that the head could be approximated to the chest. Both trapeziis were missing. On the right the accessory nerve had been cut and on the left a muscle section had been performed. The buttock was held anteriorly. As a result of the former operations there was paralysis of all the foot and toe flexors and extensors on the right side. Beyond the paralysis and sensory disturbances, due to operation, no signs of pyramidal tract involvement occurred.

The author made a diagnosis of dystonia musculorum or torsion spasm, though the possibility of a functional condition was considered. On July 25, 1917, he was operated on, the deep muscles of the neck being severed. Death occurred a few hours later. The postmortem examination showed that the internal organs were normal.

In the two cases reported, the chief findings were muscle spasms, in the first case beginning in the neck, in the second case occurring first in the legs and after a lapse of ten years involving the neck muscles. The functional possibility, according to the author, could be dismissed. He believes that the two cases may be placed in the group of dystonias because of the lack of pyramidal tract involvement, the lack of a reflex spasm and lack of sensory changes. This is in accord with the ideas of Förster and Babinski. Oppenheim refers to this same possibility. Thomalla reports postmortem findings in a case of dystonia which resembled the picture of a Wilson's disease. This has also been reported by Wimmer and Neel.

In the author's second case there was no special striate pathology, although there was a distinct anatomic change. He believes that his case disproves the psychogenic theory, although the possibility of affective changes and influences may still be present as in chorea.

Cassirer believes that torticollis may be a form of dystonia. However, an hysteria may simulate the picture so closely that only the most careful study can differentiate the condition. Whether the pathologic picture is constant remains to be determined.

MOERSCH, Rochester, Minn.

THE TREATMENT OF BRAIN TUMORS. WALTER E. DANDY, J. A. M. A. **77**:1853 (Dec. 10) 1921.

The author deals, not with a new form of treatment, for there can be, at least for the present, only one treatment, namely, surgical, but rather with an intensive development of this field, largely by the innovation of new diag-

nostic methods and also by an entire reconsideration of old time-worn and unpractical operative procedures, and the institution, in their stead, of surgical efforts directed solely to the eradication of the cause.

The author states that every tumor can and should be localized at once, and a large percentage can be removed in the earlier stages. A great number of brain tumors are infiltrating. Their removal should be made by including the extirpation of some of the healthy brain tissue, since many areas of brain permit such removal without injury.

Decompression is only a palliative form of treatment and is never performed with hope of curing the patient of a brain tumor. There are two types of decompression, subtemporal and occipital, and these procedures may occasionally give relief. They are attended with a certain operative risk, and on exploring the brain in the presence of an old decompression one finds a certain amount of damage to the underlying brain tissues, which can never be repaired. While the decompression is supposed to relieve pressure, it is at once replaced by an increase of intracranial fluid made possible by increase of the lateral ventricle. The author advises against lumbar punctures and advocates ventricular puncture in an attempt to relieve intracranial pressure. He states that the radical treatment of brain tumors depends on: (1) early diagnosis, (2) precise localization, (3) accurate and adequate operative approach to the tumor with the object of (4) removing the tumor in toto if possible, and (5) the production of the maximum palliation at the same operation if the tumor cannot be removed.

The conception that brain tumors are rare is erroneous. This is in large part due to a mistaken and incorrect diagnosis, and to the varied manifestations which make the diagnosis confusing and difficult. In the Johns Hopkins Hospital, brain tumors rank third in frequency, being exceeded only by tumors of the breast and uterus. In every case in which careful anamnesis, neurologic and roentgenologic examinations are of no avail (and this group comprises half the cases of brain tumors), the tumor can be diagnosed and located or its existence eliminated by cerebral pneumography. The author does not wish to convey the impression that air is to be injected into the brain of every patient regarded with suspicion, but that in every case in which a careful anamnesis and neurologic and roentgenologic examinations are of no avail, a neurologist or neurologic surgeon of large experience can differentiate the vast majority of cases of tumors from other lesions, and he urges the use of pneumography only when imperative and when all other means fail to aid in a diagnosis of localization.

The author says that he has had opportunity in more than 200 injections to locate tumors in every part of the brain, and has yet to fail to make an accurate localization; nor has he failed to find the tumor at operation. Some of these tumors have been far below the surface of the brain, in fact so far below that there has not been the slightest change in the surface of the cerebral or cerebellar convolutions or sulci to suggest the presence of a tumor. In other words, the evidence from cerebral pneumography has been so absolute that the author has been sufficiently certain of the location of the tumor to make a transcortical incision of varying depth until the tumor has been exposed at the expected location.

In his summary the author states that in order to obtain the best operative results, brain tumors must be diagnosed and localized in the earliest stages. Decompressions performed according to routine are among the most harmful and indefensible operations in surgery and should never be performed for

unlocalizable tumors. They should be performed only as a last resort—when the tumor cannot be removed, and then only after the location of the tumor is known, for in one half of the cases of brain tumor, no good can possibly be derived from a decompression. They are the exact equivalent of giving morphin for abdominal pain; the symptoms are masked until it is too late. Scientific accuracy must supplant guesswork in diagnosis and in directing the treatment. Early and accurate localization and thorough operative treatment will eliminate all unnecessary and harmful operations. The treatment of brain tumors can only be a direct eradication of the cause—prompt and efficient. He calls attention to the value of pneumography as a means of early diagnosis and states that he has been successful in 200 consecutive cases. He also makes a plea to abolish the use of palliative decompressions and employ more radical surgery.

While the results obtained by pneumography are quite astounding, I feel that the author is stressing a very important point when he pleads for earlier diagnosis and more radical surgery. I believe that there is a certain group of diffuse infiltrating gliomas that are better if not operated on. Decompression should be used only as a last resort; even that procedure has proved of no value in the presence of a rapidly increasing choked disk due to an internal hydrocephalus.

ADSON, Rochester, Minn.

CONTRIBUTION TO THE MORPHOLOGIC STUDY OF THE THYROID GLAND IN EMYS EUROPAEA. SANTE NACCARATI, J. Morphol. **36:** 279, 1922.

In *Emys europaea* the thyroid is a single medial organ of spheroid form and pinkish color, located in the cavity of the arch formed by the truncus innominatus. The thymus, when it exists, is a long, double, light gray organ, located in front of the carotids, with which it is in close contact, at the point of junction of the neck with the thorax. The volume and weight of the thyroids of *Emys europaea* are very variable, due to the size and age of the animal. In adults weighing about 275 gm. the thyroid has an average weight of 0.025 gm. In general, 100 gm. of body weight corresponds to about 10 mg. of thyroid. In an animal of 300 gm. the maximum diameter of the gland is about 5 mm. The gland is a little to the right of the middle. In front it is separated from the thoracic wall by a tough, transparent, lamellar connective, continuous below with the pericardium and surrounded above by the large vessels of the neck. The rear wall of the gland is in front of the trachea but not in contact with it. In *Emys europaea* the trachea divides into two bronchi a little above the thyroid, and in *Testudo graeca* the division occurs much higher near the base of the tongue.

The thyroid is highly vascularized, the blood flowing to it through the two superior and the two inferior thyroid arteries. The inferior pair are short, issuing from the truncus innominatus, and penetrating the gland at right angles, passing through its outer inferior margin. The superior arteries are longer and thinner; they branch from the carotids, turn downward and inward, and issue in the outer superior margin of the thyroid gland. These arteries are sometimes missing. There are many variations in them. The veins originate in the form of fine branchlets traversing the vesicles, composing a network on the surface of the gland, from which issue the principal veins; the latter unite with the accessory pectoral veins and empty into the subclavian vein formed by the confluence of the jugular and axillary veins. The

lymphatics are numerous, arising as small vacuoles between the cells lining the vesicles. The innervation of the thyroid is by the sympathetic, the fine non-medullated fibers accompanying the arterial ramifications. The vagus also sends two fine branchlets into the gland through the laryngeal nerves.

The histologic structure resembles that of other vertebrates. Externally there is a fibrous connective-tissue capsule containing occasional pigmented cells. From this capsule issue numerous connective-tissue septums, forming a network, enclosing the vesicles. These vesicles are irregularly rounded, and are lined with simple cuboidal epithelium. In the vesicular cavity is the colloidal fluid, an amorphous, homogeneous substance. The interior surface of the epithelial cells has a broken appearance. The protoplasm is homogeneous and contains fine grains. The gland is subdivided into lobules by connective-tissue septums. The blood vessels, lymphatics and nerves run into the intervesicular and interlobular septums forming a complicated network. The intervesicular substance is scanty, consisting of areolar connective-tissue, elastic fibers and capillaries. The granules of secretion appear to be larger and less numerous than the granules of fat and the mitochondria. They stain red when stained according to the method of Galeotti.

WYMAN, Cambridge, Mass.

SURGERY OF THE TRIGEMINAL TRACT. CHARLES H. FRAZIER, J. A. M. A. **77**:1387 (Oct. 29) 1921.

The author reviews briefly the history of the development of surgery of the trigeminal tract. J. Ewing Mears of Philadelphia was the first to propose the removal of the gasserian ganglion. In 1891, Hartley of New York first performed this operation, by the so-called Hartley-Krause method. The technic was considered to be a hazardous, adventurous procedure, and at that time was associated with a serious mortality. In the Transactions of the American Surgical Association, in 1896, Tiffany published a number of cases with a mortality of 22 per cent. DaCosta in his "Modern Surgery," placed the mortality between 10 and 17 per cent. The author states that in his last 177 consecutive operations he had only one operative fatality.

During the period from 1891 to the present, the peripheral operations on the terminal branches of the several divisions have been abandoned, and alcoholic injections have taken their place. During the same period operations on the gasserian ganglion have been replaced, with trivial exceptions, by operations on its sensory root. The procedures which the author included in the title of this communication under "The Surgery of the Trigeminal Tract," are: (*a*) subtotal resection of the gasserian ganglion; (*b*) resection of the sensory root, subtotal; (*c*) resection or avulsion of the sensory root, total, and (*d*) preservation of the motor root.

In his discussion of subtotal resection of the gasserian ganglion he says that it is not necessary to resect the ganglion if the sensory fibers are divided posteriorly to the ganglion. The approach for the various operations on the ganglion is the same, and complications such as facial paralysis, etc., are practically nil. The author believes that facial paralysis can be avoided by using the flap incision. He has performed 121 consecutive operations, none of which have been followed by facial paralysis.

He states, further, that it is possible to perform a subtotal resection of the sensory root, and by leaving one of the inner fasciculi intact it is possible to prevent an occasional atrophic keratitis. He believes that it makes no dif-

ference whether the sensory root is avulsed or resected. The physiologic results are the same, and one procedure can be as readily executed as the other. The most recent modification of the radical operation concerns the conservation of the motor root as this prevents a depression over the zygoma, owing to the atrophy of the temporal muscle. It prevents the pull to one side of the mandible on opening the mouth, owing to the preservation of the nerve supply to the temporal internal masseter and pterygoid muscles, this being extremely important if the patient should happen to have double trifacial neuralgia.

In his conclusion the author says that it is just twenty years since the sensory root operation by Spiller was first performed. It has more than fulfilled the claims of its sponsor, and is safer than a gasserectomy—with all the assurance of permanent relief. In these two decades the modifications of the technic in minor details have been made from time to time, until today the operation might be said to be a finished product, the author himself having operated on 221 patients with only two recurrences, and these should not be charged to the principle underlying the sensory root operation, the recurrences being due to the failure in dividing all of the sensory root fibers.

In discussing Dr. Frazier's paper, which was read before the Section on Surgery at the Seventy-Second Annual Session of the American Medical Association in June, 1921, Gilbert Horrax of Boston reported 345 consecutive cases in which the patients were operated on for trifacial neuralgia without one death. He took exception to the subtotal resection of the sensory root, feeling that trifacial neuralgia is a progressive disease and will sooner or later, in a large percentage of cases, involve the ophthalmic division. The results from the radical operation have been most gratifying; it has relieved patients of pain and agony, probably the most severe that the body is called on to endure. The operation has been improved so that it is attended with an extremely low mortality, and the results presented by both Frazier and Horrax at Brigham Hospital are most enviable. On the other hand, one must not be too cautious, and fail to relieve a sufferer or patient who is a poor surgical risk.

I have observed numerous patients who have received repeated injections of alcohol until the injections failed to give relief and a radical operation was the only procedure remaining, even though it was not unattended with a great surgical hazard.

ADSON, Rochester, Minn.

PRIMARY NEUROMERES AND HEAD SEGMENTATION. HORACE W. STUNKARD, J. Morphol. **36**:331, 1922.

In the early neural groove stage of Amblystoma, faint alternating lighter and darker areas may be seen, but these are so irregular as to preclude interpreting them as segments. After the anterior parts of the neural folds have risen prominently, faint transverse grooves appear in the anterior part of the medullary plate, but they are inconstant in number and irregular in position. Sometimes similar divisions appear posterior to these, but they are less distinct. Some of the grooves shift slightly or fade out entirely and others appear in different positions. Divisions of the neural plate caused by these transverse grooves could not be clearly demonstrated in sections. With the appearance of the grooves the mesoderm is assuming a segmented condition, and the formation of the grooves is due to the formation of the mesodermal somites. It is possible that they are also due to pressure produced by the multiplying cells and the infolding of the neural crests. In the lateral ridges

a beaded appearance is sometimes present, but it is not regular in size or arrangement. The number varies from two to fifteen on a single side, and there is no correspondence between the lobulation of opposite sides. Sections of the crests showed no segmentation, the lobulation being due to centers of rapid cell proliferation. No relation between the median divisions and the three primary brain vesicles could be determined.

In the chick no indication of anything that could be interpreted as segmentation could be observed in the primitive streak or before the neural folds were clearly outlined. Lobulated irregularities are formed along the elevated margins of the medullary plate and are present in most embryos up to the closure of the neural tube. They are irregular in number and do not correspond in two sides of the same individual. They vary in size and are probably due to differences in the rate of cell proliferation along the expanding wall of tissue. As the neural crests increase in size faint lines appear in them, but they are irregular and variable. Faint constrictions appear on the external surface of the neural folds, but they are irregular in number and position. They do not regularly encircle the encephalon and the number of constrictions is different for two sides of it. Internal grooves do not regularly correspond with external constrictions. After the closure of the neural tube there are clearly six segments anterior to the auditory invagination. In these divisions there is present the definite cell arrangement distinguishing true neuromeres. In the open neural groove there is no suggestion of a segmental condition.

The so-called "primary metamerism" of chick and Amblystoma embryos is based on incorrect observation and cannot be accepted.

WYMAN, Cambridge, Mass.

INTRACRANIAL AEROCELE FOLLOWING FRACTURED SKULL. GILBERT HORRAX, Ann. Surg. **73**:18 (Jan.) 1921.

The author reviews briefly a case of intracranial aerocele resulting from trauma to the skull, as well as some cases previously reported.

A girl, 19 years of age, was admitted to the Peter Bent Brigham Hospital in September, 1919. She had been injured on June 9, 1919, and was taken to a hospital. A roentgenogram at that time showed a compound comminuted and depressed fracture of the skull extending from near the vertex slightly to the left of the midline, downward and forward to the occiput, forward through both orbits, and presumably through the base of the skull. All loose bone fragments were removed at operation and hemorrhages were controlled. There was considerable laceration and loss of substance in the left frontal lobe. The wound was closed, a small drain being left in place. The postoperative course was uneventful.

The patient came to the Brigham Hospital to the service of Dr. Harvey Cushing three months after her injury because of weakness of the right side of the face, blindness of the right eye, deafness of the right ear and loss of the sense of smell. Neurologic examination verified the complaints. A roentgenogram of the skull showed an area of decreased density corresponding to the palpable defect in the cranium. It extended from the left frontal sinus upward for a distance of 6.5 cm., and its greatest diameter was 4 cm. On comparing this roentgenogram with others which the patient had brought with her, it was evident that another and somewhat different area of decreased density had been present at an earlier date. The previous plates had been taken two months before her admission to the Brigham Hospital and one

month after her initial injury and operation. At this time the plates showed that the area was due to the cranial defect. There was also a lobulated shadow of decreased density underlying the bony defect, which looked like a conglomerate mass of bubbles, the picture indicating clearly that this irregular area represented an accumulation of air within the cranium. Its extension backward within the cerebral tissue of the left frontal lobe for a considerable distance was shown by the lateral plate. The origin of this gaseous matter—presumably air—was unquestionably a crack in the frontal sinus.

The author calls attention to the fact that there are few accounts in the literature of such air-containing cavities in the brain. This seems strange as the condition must occur fairly frequently following gunshot wounds and other cranial injuries. After intracranial operations there must often be inclusions of air which lie surrounded by cerebral substance, either covered by dura or below places from which the dura has been purposely removed. Apparently no specially significant features are associated with such inclusions, either in the way of subjective sensations, or in the manner of wound healing, except their possible relation to subsequent "traumatic cysts," as mentioned by Potter.

Seven cases were recorded. Four of the patients died as a result of the injury or its complications. Recently it has been shown experimentally by Dandy that air can be introduced into the cerebral ventricles or into the spinal subarachnoid space, and this fact has been utilized clinically for the confirmation or determination of certain pathologic intracranial processes. In Dandy's experience, no deleterious results have followed such injections, except an occasional headache, which is easily relieved by ventricular puncture.

In the author's case, the skull injury occurred on June 9, 1919, but no reference to air within the cranial cavity was obtained until the plates of July 8, 1919, were taken. Between this time and Sept. 2, 1919, when the final plates were made, the air had disappeared and had caused no serious symptoms so far as could be learned from the history. No operative measure seemed indicated, and the patient was consequently discharged.

ADSON, Rochester, Minn.

THE DIAGNOSIS OF BRAIN TUMORS BY THE BÁRÁNY TESTS. WITH REPORTS OF CASES PROVED BY OPERATION OR NECROPSY. LEWIS FISHER, J. A. M. A. **78**:1515 (May 20) 1922.

The author emphasizes the value of a complete ear examination by the so-called Bárány test as an aid to the neurologist and neurosurgeon. He believes that such an examination, when made by an experienced otologist, will frequently clear up many of the difficult and perplexing cases. He has found that tumors located in the cerebellopontile angle give the most constant complex of findings, indeed, so constant that in a number of cases in which neurologic data were most confusing and even indicative of lesions elsewhere, these tests were the only means of localizing the lesions accurately.

The typical picture of a cerebellopontile angle tumor is as follows: Total deafness with no response from the horizontal and vertical semicircular canals of the affected side. On the opposite side the hearing is good; the vertical semicircular canals produce no response at all, while the horizontal canal produces good nystagmus, vertigo and past pointing. The nonresponsive and deaf ear on the affected side is accounted for by the neoplasm destroying the eighth nerve, while the absence of responses from the vertical semicircular

canals of the opposite side is probably the result of pressure. He believes that in tumor in the cerebellopontile angle these tests are practically absolute.

In tumors of the posterior fossa vertigo and past pointing responses are particularly affected, while the eye responses are either normal or exaggerated. In lesions located "higher up," the Bárány tests will also be of value. In supratentorial lesions the vertigo responses are found to be either normal or subnormal, while the past pointing is exaggerated both in extent and duration. In cases of neoplasm of the pituitary body the first effects of the pressure are exerted against the vestibulo-ocular tracts. In these cases the examination reveals an exaggerated nystagmus, but normal vertigo and past pointing. He believes that the Bárány tests are of great value in differential diagnosis between a subtentorial and supratentorial lesion and that these tests are also helpful to a lesser degree in lesions in the middle or anterior fossa.

NIXON, Minneapolis.

FRACTURES OF TRANSVERSE PROCESSES OF THE LUMBAR VERTEBRAE. GEORGE G. DAVIS, Surg., Gynec. & Obst. **33**:272, 1921.

The author calls attention to fractures of the transverse processes of the lumbar vertebrae, a lesion of not infrequent occurrence, but one that is frequently overlooked. With the aid of the roentgen ray, intensifying screens, and especially the Potter-Bucky diaphragm, many cases formerly diagnosed as "sprained back," are now recognized as fractures of the transverse processes. Writers on this subject have expressed considerable difference of opinion as to the etiology. The cartilaginous vertebra is ossified from three primary centers, two for the vertebral arch and one for the body. The ossific granules appear first in the situations where the transverse processes afterward project, and spread backward to the spinous process, forward into the pedicles, and laterally into the transverse process. At birth the vertebra consists of three pieces: the body and the halves of the vertebral arch. Before puberty no further changes occur, except a gradual increase of these primary centers, the ends of the transverse processes being cartilaginous. About the sixteenth year, two secondary centers appear, one for each transverse process. These secondary centers fuse with the transverse process at about the age of 25. From this secondary center the transverse process of the first lumbar vertebra is sometimes developed as a separate piece which may remain permanently ununited with the rest of the bone, thus forming a lumbar rib. Some believe that fracture of the transverse process of the lumbar vertebra is due to a weak point between the transverse processes and the rest of the vertebrae.

The author reports eight cases and illustrates the article with numerous roentgenograms. The symptoms of fractures of the transverse process are definite, backache being the first symptom. The pain, which is well localized, constant and nonradiating, is exaggerated by any motion that changes the line of the weight of the body. Rising from the incumbent to the sitting position or from the sitting to the erect position increases the pain. Flexion and hyperextension of the spine, and lateral bending, both toward and from the injured side, cause pain. In no position other than lying relaxed in bed is the patient free from pain. Bending toward sometimes causes more pain than bending from the injured side. Muscular rigidity and a point of exquisite tenderness over the fractured process are noted. The pain in the back is not accompanied by any neurologic symptoms. In some cases, however, the symptoms are so slight that the patient goes back to his occupation in a few weeks complaining very little.

The diagnosis is made by the history of a fall or injury to the back resulting in an area of localized tenderness lateral to the median line of the spine. As is the case in fractures of long bones this localized tenderness is the most reliable sign. The roentgen ray, of course, will show the fractures. Many cases which would not be recognized by the roentgen ray have doubtlessly been overlooked and considered only as sprains.

CONCLUSIONS

Indirect violence plays the most important rôle in these fractures.

The occurrence is noted in patients of advanced years, men beyond the age at which we would expect separation of the secondary ossific centers from the primary ossific centers of the transverse processes.

The condition is often associated with osteo-arthritis.

ADSON, Rochester, Minn.

THE NATURE OF MENTAL DEFICIENCY. A. F. TREDGOLD, J. Neurol. & Psychopath. **2**:311 (Feb.) 1922.

The highly suggestive method of study here advanced is not as inelastic and dogmatic as might appear from this abstract. A brief résumé of mental evolution arranged diagramatically in four stages is given: (1) the unconscious, instinctive adjustments of the primitive vertebrate; (2) the higher mammalian level; (3) primitive social man, and (4) civilized man. At this last level perception has evolved into "learning," apperception into "wisdom" and feeling into "sentiment." Each of these three is subdivided, tentatively, into three subheads: Learning includes (1) complex concepts, ideation and imagination; (2) complex abstract ideas, and (3) complex symbols. Wisdom includes (4) deliberation, discrimination and reasoning, (5) volition and resolution, (6) prudence, planning and inventiveness. Sentiments are divided into (7) esthetic, (8) religious, and (9) social and moral.

Examples of mental deficiency are then analyzed on the basis of these nine elements. Legal mental deficiency is found to depend essentially on apperceptive defect. The idiot, imbecile, low grade and high grade moron (the author uses the English equivalent, feebleminded) correspond practically with arrest of development in the four different levels mentioned in the foregoing, but with special deficiency in apperception. The author is careful to point out that development is irregular and that these degrees of deficiency are not simply atavisms.

In addition to these committable types, there are many examples of mental deficiency which may or may not permit social adjustment, largely dependent on the complexity of the social environment and the degree of apperceptive endowment. Thus the "subnormal" or simple person who may just get by shows a general deficiency in level 4 but full endowment at level 3. The person with good learning and sentiment but lacking in wisdom is "the moral, conscientious, learned fool." Another type, often practically successful, lacks learning and sentiment but has plenty of good "common sense" or wisdom. The potential criminal, deficient in moral, and possibly also in religious sentiment, is kept from crime by fear of consequences for he possesses learning and wisdom. Finally, the "moral imbecile" or inherent criminal has much learning but neither wisdom nor sentiment. This last type is also legally committable under the British Mental Deficiency Act of 1913.

SINGER, Chicago.

THE PATIENT AND HIS ATTITUDE TOWARD HIS NEUROSIS. Douglas A. Thom, Ment. Hygiene **6**:234 (April) 1922.

Dr. Thom presents a broad and useful differentiation of the neuroses based on the attitude of the patient toward his illness. To the active group belongs the person who seeks refuge in his neurosis. He is apt to be inherently unstable; the motive is obvious to the psychiatrist and the symptomatic expression is crude. On the other hand, the passive type is overtaken by the neurosis. He is more likely to be potentially stable; the purpose is obscure and the symptomatic mechanism intricate largely because the original stimulus "is not in operation in conjunction with the symptoms, but only the emotion that was attached to the primary experience." During the war the active attitude was represented by the anticipatory neurosis and now by the compensation reaction while the passive attitude has its prototype in the amnesias or psychasthenias. The practical distinction lies in the prognostic hopefulness of the former and the doubtful outlook for the latter.

In formulating therapeutic suggestions Thom recalls the now well-known differences between prewar and postwar treatment conditions. During active hostilities the apparently insurmountable difficulties were more than overbalanced by the intrinsic advantages of the situation. The psychiatrist in the line of combat was dealing with a soldier and not a pensioner; he had authority; he could appeal to patriotism and military traditions. Finally, and occasionally even consciously, the choice of the patient was apt to be in favor of a return to duty as against monotonous hospital life. In civil life the odds are rather against the psychiatrist. There is no legal or military control; a soldier may refuse treatment; there is no patriotic urge, and there is the glamour of the pension. The present problem relates largely to the active group, in which all sorts of environmental circumstances, such as, for instance, marital difficulties or economic stress, which are entirely foreign to the war, may precipitate the neurosis.

The author is opposed to prolonged hospitalization. He favors the outpatient neuropsychiatric clinic, which with its medical, psychologic and social service adjuncts offers the best opportunity to rehabilitate the dangerously large number of actively neurotic ex-soldiers.

Strecker, Philadelphia.

THE REACTIONS OF AMBLYSTOMA TIGRINUM TO OLFACTORY STIMULI. J. S. Nicholas, J. Exper. Zoology **35**:257, 1922.

Observations were made on both larvae and adults of *Amblystoma tigrinum*. Four series of larvae were used: (1) larvae with the optic vesicles removed; (2) larvae with the nasal placodes removed; (3) eyeless and noseless larvae, and (4) normal larvae. A corresponding series of adults was used, namely, blinded, nose-stopped, both blinded and nose-stopped, and normal animals. Earthworms, beef-juice and strips of beef were used as the stimulating substances.

General observations on the growth and behavior of larvae operated on show that the visual sense is the primary sense used in obtaining food. When motionless food substances are the only ones present, the olfactory apparatus functions to a greater extent in eyeless larvae than it does in normal animals. The experiments on adult animals indicate that while the eye is the most important agent in obtaining food, with the nose alone the animals are capable of detecting and locating definite food substances. When the animals are tested

in darkness the evident retardation in the time of reaction is due to the dependence of the animal on the sense of sight. After the removal of the eyes of the animals they become accustomed to use the olfactory organ only, and in this way the remaining sense organ is correlated to the needs of the animal. Experiments performed with diffusing and nondiffusing substances demonstrate the fact that an animal possessing the optic sense is stimulated by nondiffusing substances, while those possessing the olfactory sense are stimulated by diffusing substances. Odor streams involving the use of a number of substances elicit no further response on the part of the animal unless the substance used possesses irritating properties, in which case the animal responds by a decided motor reaction. Responses to motionless test substances in air show that the animal can find food substances, although the reaction time is longer than if the animal and the test substance are submerged. The experiments indicate clearly that there is a definite olfactory sense in both the larvae and the adults of *Amblystoma tigrinum*.

WYMAN, Cambridge, Mass.

THE SOCIAL SIGNIFICANCE OF DEMENTIA PRAECOX. EDITH M. FURBUSH, Ment. Hygiene **6**:288 (April) 1922.

Statistics are usually uninteresting and often deceptive, but sometimes the lesson they teach is so impressive that they demand the closest attention. This is true of the statistical study of dementia praecox contributed by the statistician of the National Committee for Mental Hygiene. Any doubt as to which psychosis furnishes the largest and most serious institutional problem is at once removed by the observation that the permanent dementia praecox population of state hospitals is at least 130,000 which is increased annually by 13,000 new cases. On such a basis, this form of mental disease is twice as important as tuberculosis. In the New York institutions 73 per cent. of the patients come from urban centers; the incidence is higher among the foreign-born and the racial distribution among those of native birth shows a preponderance in the Irish (16 per cent.), Hebrew (12 per cent.) and German (11 per cent.). Peculiar clinical interest should attach to the fact that 32.6 per cent. of the patients in the praecox group die of pulmonary tuberculosis. Even the quite conservative economic conclusions which are given are staggering in their magnitude. The annual economic loss to the nation which is estimated from the cost of maintaining patients plus the loss of their earning power is placed at $123,650,000! In this connection it may be well to remember that the hospital residence time is longer than in any other psychosis, and in twenty-six of every 100 schizophrenic patients amounts to twenty years or longer.

It is a rather serious commentary on psychiatry that concerning the etiology, diagnosis, prognosis and treatment of dementia praecox, our information should be most thorough and exact only in respect to the gloomy outlook for the patient. The natural defense is that funds are not available for research as they are for the study of tuberculosis or cancer. It is possible, however, that the effort to awaken the public has been somewhat lacking in determination. The presentation of the problem in the practical terms of Miss Furbush's article is a long stride forward.

STRECKER, Philadelphia.

DEMENTIA PRAECOX AND SYPHILIS. RANSOM A. GREENE, Am. J. Psychiat. **1**: No. 3 (Jan.) 1922.

Greene investigated the frequency of syphilis in dementia praecox. The statistics are rather surprising. Of 495 patients with schizophrenia included in 2,117 hospital admissions, only eight had syphilis. A more extended search of the hospital records discovered twelve syphilitic patients in the entire dementia praecox group. An interesting suggestion is that as a part of the characteristic seclusive makeup onanistic or masturbatory excesses occur rather than promiscuous cohabitation, and thus the psychopathology of the psychosis automatically protects the patient from syphilitic infection. Naturally, with the evidence submitted one must concur in the conclusion that syphilis is not to be considered a direct causative factor of dementia praecox.

STRECKER, Philadelphia.

PROGRESSIVE LIPODYSTROPHY: REPORT OF CASE. AUGUST STRAUCH, J. A. M. A. **78**:1037 (April 1) 1922.

The case reported is that of a woman, aged 27. Between the ages of 11 and 17 she had had a rather full figure, and the lower extremities were somewhat stout. At 17 her weight was 150 pounds (68 kg.). From the age of 19 her face and neck became progressively emaciated and at 20 the chest, arms and upper part of the abdomen were similarly involved.

The increase of adipose tissue occurred only in the lower part of the body. Her height was 5 feet, 3½ inches (160.8 cm.) and her weight was 149 pounds (67.5 kg.).

The condition in this case corresponds to that described by Simons in 1911 in which there was a symmetrical atrophy of the subcutaneous fat tissue of the upper part of the body and, a few years after the onset, in most cases an excessive accumulation of adipose tissue in the gluteal region, on the thighs and also on the rest of the legs. As evidence of this anomalous condition it is noted that the circumference of the waist line and the thigh were the same in the patient reported. The author gives complete measurements for comparison with other cases reported.

NIXON, Minneapolis.

Society Transactions

NEW YORK NEUROLOGICAL SOCIETY

March 7, 1922

FOSTER KENNEDY, M.D., *President, in the Chair*

A CASE OF PSEUDOTUMOR, WITH NECROPSY FINDINGS. DR. BEATRICE FAIRBANKS (by invitation).

In February, 1921, a student, 21 years old, developed headache, vomiting, dizziness and weakness, which increased in the succeeding months, accompanied by transitory aphasia, numbness, confusion and slight disturbance of consciousness. Later diplopia appeared.

Dr. Ward Holden examined the eyes in June, 1921, and said that the fields indicated pressure on the chiasm. He found the pupils slightly irregular, with sluggish reaction to light. There was slight divergence of the eyes to near fixation. A crossed diplopia was present with red glass, with images close together and an equal distance apart, both in looking to the right and left. Vision was 20/40 in the right eye and 20/20 in the left. In each temporal field there was a long oval scotoma extending from near the fixation point to beyond the blind spot. Movement of the fingers was seen in these areas, but the scotoma was absolute for a 5 mm. test object. The fundi showed a bilateral papilledema with many hemorrhages and patches of exudation. The top of each disk was plus four and the retinae zero.

Clonus was present on the right side but not on the left. This was also true of the Babinski sign. There was more power on the left side than on the right. The patient could not remember events of the previous day.

At this time radiographic study of the skull showed a suggestion of intracranial pathologic changes and displacement of the pineal gland downward. The spinal fluid was not examined, but the Wassermann reported was negative. In July Dr. Elsberg performed a subtemporal decompression; nothing abnormal was noted in the dura, but considerable subdural pressure was present. Later in August further decompression was done, after which a left hemiplegia developed. In October the patient became blind, and was treated with radium at the General Memorial Hospital. From this time he suffered tremendous thirst necessitating drinking several liters a day. There was great cranial herniation. Spinal drainage was performed eight times. One week before death the patient had a transitory convulsion, having great respiratory and cardiac difficulty, and two days later acute edema of the entire left side set in. The patient was cheerful and optimistic, but very forgetful, and remained oriented until the last.

Pathologic Findings: The whole brain was hardened in formaldehyd. Externally in the cortical region, corresponding to the right island of Reil, there was a cavity, into which it was possible to introduce the forefinger, with extensive roughening and laceration of the cortex in the vicinity, and extending upward and forward over the rolandic area. On section the lesion was

found to communicate with the posterior horn of the lateral ventricle, impinging slightly on the external border of the lenticular nucleus, and extending as far forward as the anterior horn, sloping outward so that at its most anterior point it was found only in the plane of the cortex. The vertical diameter was about 2 cm. at its widest point.

The macroscopic appearances were not those of a glioma with hemorrhage and necrosis, as we expected. It is always possible in these tumors, however rapid the degeneration has been, to find a zone of the familiar pearly color and gelatinous consistency between the necrotic area and the normal tissue. On the other hand, although the brain substance was normal in color and consistency, the edges were ragged to a degree incompatible with a porencephaly or a congenital hydrocephalus, where the convolutions usually dip smoothly down into the cavity. There was no evidence of a cyst wall, which is a perfectly definite structure microscopically, and there were no indications of abscess. Neither did the naked eye appearances suggest a gumma, which is usually surrounded by a distinctly hyperemic zone.

Microscopically we examined sections from blocks taken from all points of the circumference. Professor Ewing examined them thoroughly, and confirmed my opinion that there was no tumor present. Haidenhain's iron alum and ordinary hematoxylin gave the most useful results. All sections showed a slight increase in the number of large cells of undoubtedly glial origin. The small ones appeared to be lymphocytes. If the glial cells were small and of the type frequently found in the so-called glial sarcoma, we should expect to find transition types between them and the large cells, which were not present. There was a thickening and a slight increase in the cells of the subpial glia, a proliferation of the small vessels and a thickening of the large ones. There was a general perivascular infiltration, more suggestive of a chronic inflammatory condition than a neoplasm, particularly a gliomatous one, where the vessels are liable to be thin-walled and easily ruptured. There were no compound granular corpuscles.

I think we can eliminate the question of tumor. There remain lethargic encephalitis, syphilis and pseudosclerosis. However, I do not think we need to consider encephalitis, as the sections nowhere displayed the typical cuffing of the arteries which would be inevitable in a case of such long standing. Against the diagnosis of syphilis are the negative Wassermann reaction and the social history of the patient. In favor of the diagnosis there are the pathologic appearances which suggest an early stage, not more than secondary, which might fail to give the reaction, and the clinical history, points of which, such as the recurring diplopia, are rather suggestive of syphilitic disease. I sent the sections and the history to Dr. Greenfield, pathologist at the National Hospital, London. Although unable to make a diagnosis, he thought the lesions most probably syphilitic in origin. As to pseudosclerosis, the rapidity and course of the disease in this case are entirely opposed to what we know of this pathologic process. On the other hand, we know almost nothing of the factors controlling it, except in Wilson's disease, in which the fons et origo mali would appear to be the liver, and there is now no evidence that a similar process might not represent the reaction to some other primary infection. If so, it probably began in the island of Reil.

Microscopically, the abrupt transition between the normal tissue and the cavity, the type of large cells, and the perivascular gliosis are reminiscent of

the description Wilson gave of those cases of lenticular degeneration which he personally examined. The process must have been a slow one, owing to the extreme passivity of the tissues surrounding the cavity, possibly supervening on some slight congenital defect, and the tumor symptoms are largely referable to the hydrocephalus resulting when the cavity extended into the ventricle.

DISCUSSION

DR. SMITH ELY JELLIFFE: It would be presumptuous at this time to hazard a suggestion as to the diagnosis. There will be more to say when serial sections are made. These may show foci in which a serous exudate has pushed through and destroyed the tissues in other portions of the brain.

DR. FOSTER KENNEDY: Perhaps the difficulty which Dr. Fairbanks finds may be due to the fact that radium had been heavily used, and this treatment may have destroyed typical cells. This has not perhaps been sufficiently taken into consideration.

DR. FAIRBANKS, closing: I have not studied the effects of radium on the human brain. These results are not compatible with those I have seen in radiumized dogs. I do not think it would be possible for one type of cell to be so completely destroyed without affecting the others.

IS THE STOMACH A FOCUS OF INFECTION IN THE PSYCHOSES?

NICHOLAS KOPELOFF, PH.D., New York State Psychiatric Institute (by invitation).

DR. KOPELOFF presented a critical analysis of this question as determined by the Rehfuss fractional method of gastric analysis. The conclusion arrived at on the basis of the experimental evidence advanced (illustrated by lantern slides) was that the bacterial content of the stomach is influenced by the saliva and that the Rehfuss method of fractional gastric analysis cannot be considered an adequate criterion in determining whether the stomach is a focus of infection.

Quantitative as well as qualitative studies were made of the bacteria found at different stages in the digestive process, the fractional method of gastric analysis being employed. In order to investigate the influence of saliva on the bacterial flora of the stomach, in some experiments, a dental suction tube was kept in the subject's mouth for the removal of saliva during gastric analysis. This made possible a comparison of gastric fractions contaminated and uncontaminated by saliva. Bacterial counts showed a striking reduction in numbers in gastric fractions when saliva was inaccessible. The highest number of bacteria per cubic centimeter in a psychotic patient (manic-depressive, manic) when saliva was not removed was 48,000; when saliva was removed the highest number found was 32. Similar results were obtained with a normal person and with other patients having the same diagnosis. These data take on an added significance when it is remembered that the swallowing of saliva is particularly difficult to control in manic patients. Furthermore, it is important to note that this reduction in numbers of bacteria when saliva is removed, occurs alike in patients having low gastric acidity and in those of a more normal type.

No correlation was found between high acidity in the stomach and low bacterial numbers or vice versa. Streptococci were found associated with high, as often as with low, gastric acidity. Consequently, there seems to be no reason to attach undue importance to their presence, or therefore to con-

sider the stomach as a focus of infection. This means that another factor, the saliva, is of greater importance, determining the bacterial content, within certain limits. Furthermore, the fact that the bacterial count on the "fasting contents" is usually considerably lower than during the process of digestion, indicates that little or no multiplication of bacteria takes place when the stomach is relatively at rest. As might be expected, the micro-organisms found in the different gastric fractions with greatest frequency are yeasts, staphylococci, streptococci and members of the lactic-acid and aerogenes groups. Invariably these are found in the saliva of the same patient or in the food given. Consequently, they cannot be regarded as constituting a true bacterial flora of the normal stomach. It is of interest in this connection to note that a similar study of normal persons yielded a bacterial flora qualitatively and quantitatively similar to that found in persons with psychoses.

From these various considerations, it may be inferred that the stomach is not acting as a focus of infection, but merely as a receptacle for the bacteria poured into it. This is in agreement with the conclusion of others as a result of bacteriologic investigations, namely, that gastric acidity is sufficient to prevent bacterial development.

DISCUSSION

Dr. Smith Ely Jelliffe: This method is a valid means of approach to this problem, and can be used as a corrective way of checking up assertions made by Dr. Cotton and others. There are, however, other factors involved in the point of view taken by Dr. Cotton which are not quite covered by the observations here set forth. While I do not hold a brief for Dr. Cotton's statements, I think his point of view embraces the idea that the long-standing focal infections produce such a lowering of resistance that the coordinating factors represented by the cerebral cortex are interfered with; that is, if we are to understand the psychoses of the dementia praecox variety, about which type Dr. Cotton concentrates his work, we must grant that the cerebral cortex in its organizing capacity attempts to coordinate the activities of the various organs. If any organs, therefore, are thrown out of order or interfered with by chronic focal infections, such a degeneration must be represented in the cortex itself in its higher organizing function. If the organs which contribute to the organism as a whole are infected, the result is a lack of synthesis of their activity in the cortex. Along these lines Dr. Cotton's observations are not entirely negatived by the presentation made this evening. If we do not find a decreased amount of bacteria relative to diminished function of the stomach the observations only confirm *a priori* the conclusions that common sense would bring us to believe. I believe these facts are worthy of consideration in the study of all the psychoses.

Dr. Kopeloff, closing: I am in general agreement with Dr. Jelliffe's point of view. The material presented was only a small part of the work actually completed. We have conducted a number of experiments in regard to the influence of operative and nonoperative treatment on the psychoses. In this paper I discussed the question of stomach infection along the lines indicated by Dr. Cotton. He claims that the stomach is a focus of infection, that is, shows low acidity and presence of bacteria, and he gives autogenous vaccines on the strength of that. The next gastric analysis shows increased acidity and absence of bacteria. My work negatives these results. Other work to be reported at the American Psychiatric Association will deal with the results of operative treatment in the psychoses.

CONSIDERATIONS OF SOME EXPERIMENTAL STUDIES ON THE DEVELOPMENT OF THE NERVOUS SYSTEM. Dr. Charles R. Stockard, Cornell University Medical College (by invitation).

We shall consider in a brief and informal way some of the primary problems in the development of the nervous system.

The nervous system belongs to the general skin system, and may be called a modified part of the skin system. It is the appreciative portion of the wall or sac which separates the organism from its surroundings. The appreciative portion must be capable of affecting the underlying parts so as to call forth a response to the stimuli received from the environment. This demand seems to stand behind the evolution of the nervous system. We may scan the scale of elementary nerve arrangements as follows:

The simplest animal cell is an irritable contractile body and may in certain cases contain a fibrillar-like "nervous system."

Kleinenberg long ago recognized in the ectoderm cell of Hydra an outer sensory part and an inner contractile portion; he therefore designated it the "neuro-muscular cell."

In slightly higher forms the sensory and contractile parts apparently separate into two distinct cells connected by a fiber which passes from the superficial sensory cell to excite the more deeply placed contractile cell. In still higher forms the sensory cell becomes divided into a superficial end-organ and a deeper placed nerve cell, the cell on the surface communicating through a nerve cell with a muscle cell.

Comparable successive differentiations actually take place during the embryonic development of higher forms, as may be illustrated by the case of the vertebrate retina which is derived from the primitive ectoderm cells and becomes differentiated into the end-cells which are the rods and cones, and the ganglion cells with their various connections. In the development of these complexes it may be shown experimentally that one part may be suppressed or absent and the other parts may finally become well formed, as, for example, the end organ or retina may not develop, or may be removed, and yet the brain center cells may arise and persist.

In higher vertebrates and in man the separation of the nerve tissue from the general skin or ectoderm takes place at an early time in the embryo; in fact, the central nervous system is one of the earliest organs or systems to express itself in development, being second only to the primitive intestine, if even to that. From this early start it continues to develop and undergo change until long after birth. Thus the interval of development for the nervous system is extremely long. This fact renders the nervous system liable to arrests or developmental interferences, since any unfavorable condition occurring at any time during development acts particularly on those parts which are developing at the given time. Some element of the nervous system would, therefore, be affected at almost any time. We may now review a number of experiments that I have carried out which throw some light on this subject.

Effects of Arresting the Growth of the Primary System: Growth in general has an initial linear stage and a subsequent lateral expansion stage which takes place after the high rate of the linear impulse has been spent. If the initial linear stage of the central nervous system in a vertebrate embryo is suppressed the differentiation of the body of the individual entirely fails to occur and only an amorphous embryonic mass results which soon dies.

On the other hand, if growth is arrested or injured after the linear growth has begun, some of the lateral outgrowths, such as the optic vesicles and hemispheres, may be suppressed in various combinations, or all may be suppressed. In the latter case only a simple tubular brain develops which resembles the anterior end of the spinal cord. Fish embryos with such brains as this may develop to the stage of hatching but do not hatch. They are eyeless and deformed in other ways. In other cases tubular brains may develop with eyes or cyclopean eyes. Thus it is possible to suppress one group of lateral outgrowths, such as the eyes, and yet have another, such as the hemispheres, develop, or vice versa.

Asymmetrical Conditions and the Question of Bilaterality: If one examines the early optic vesicles and neural folds of various vertebrate embryos, it will be noted that one lateral half or side is developing slightly faster than the other. It would seem as if the two sides were somewhat independent, or rather competing with one another. In this competition the advantage of one side over the other may be the underlying cause of left-sidedness or right-sidedness. The eye on one side comes off somewhat earlier and is at first slightly larger than the other, although finally the two eyes become practically equal in normal development. In extreme cases, however, monophthalmia may result. This also is true in the development of the primary brain ventricles, which may be very small on one side. Thus a general developmental basis for unilateral arrests and malformations is clearly present in the embryonic system, and one side of the body may be well developed while the other side is paralyzed and deformed.

Localization of Future Stuffs or Parts in the Neural Plate: The early localization of materials for future structures in the neural plate of the embryo may be illustrated by studies on the eye or retina, since this is so definite a structure and becomes extremely large before undergoing normal differentiation. A number of workers had taken it for granted that since the eyes are finally lateral in position, they originally arise from lateral positions in the neural tube. Operative experiments had been conducted from this standpoint. The "lateral" portions of the anterior neural plate were cut away, and following this operation no eye developed, but no significance was laid to the fact that the cut had really removed the central as well as the lateral portion of the neural plate. In attempting to account for certain conditions shown by cyclopean eyes I was forced to assume that the earliest eye stuff must be originally located in the midline of the neural tube and it only later develops laterally from this origin. Stuffs located in lateral parts of the early neural plate become dorsomedian since this is where the lateral tissue is finally carried. Had the eye originally been lateral the optic nerve would have grown into the side of the brain and its fibers would have crossed inside instead of outside and ventral to the brain. Though median to begin with, the eye forming material develops lateral to the midplane and finally becomes divided into two definite eyes. Other parts are also similarly located in the median plane and have to shift to their final lateral positions.

Independence of Secondary Centers: The study of the eye parts of the brain have also shown that some of the secondary nerve centers are independent, in their development, of the existence of other parts of the complex organ. For example, the retina may be completely absent, there are no ganglion cells present to send their fibers into the brain, and so no optic nerves and no primary optic tracts, but the optic radiations and optic centers in the occipital lobes may be fully developed. This is shown in the brains of eyeless guinea-pigs.

Late Growth and Differentiation: An experiment which illustrates strikingly the long period of development of the brain was recently performed by Dr. H. G. Bagg, connected with our laboratory. He found that when solutions of radium emanations were injected into pregnant rats one or two days before the birth of the young, the radium affected the brain cells of the young to the extent of destroying many of them. It is well known that dividing cells are particularly sensitive to radium, and the brain at this time is injured because it has so many cells in mitosis while at this time other organs are more nearly in a resting condition. The testes are also greatly affected since here too active cell division is taking place. Thus, injurious effects of the environment may so act as to injure the development of the central nervous system from the earliest moments of development right up to the time of birth, and as all know, long after that. The variety of the stimuli which cause these injuries have little to do with the type of injury. The kind or quality of injury depends chiefly on the developmental moment when the effect takes place. Early injuries are, as a rule, more serious than later ones. For example, all of the brain cortex may become degenerated following a late injury, as with radium, and notwithstanding this, many animals continue to live.

The Endocrine Glands in Determination of Kind and Quality of Central Nervous System: Many claim that the brain develops entirely as a response to the glands of internal secretion. It is obvious that this overstates the case. The experiments mentioned in the foregoing show that many external conditions tend to decide the manner of brain development. And certainly a study of the embryology of the nervous system shows clearly that heredity, quite aside from the heredity of internal secretions, determines the general character of the central nervous system, for example, whether it shall become the brain of a tiger or of a dog, of a monkey, or of a man. Nevertheless, changes in the developmental rate of the central nervous system effect its quality and in so far as the rate of development, rate of metabolism or rate of oxidation is influenced by an internal secretion during later developmental stages, we may admit that the smaller peculiarities of brain growth and development are modified by the internal secretions. This is strikingly shown in the case of the cretin with an arrest of mental development corrected by thyroid administration. In the presence of such secretion the brain promptly responds.

The central nervous system in common with all body systems has a definitely normal rate of development. Any cause that modifies this rate to a marked degree will also modify the quality of nervous development, and the type of central nervous defect resulting depends on the developmental stage at which the interference took place and not necessarily on the nature of the irritant producing the arrest.

The same poison or mechanical irritant may be used to induce every known deformity of the nervous system if applied at different periods of development. A hundred different irritants will induce exactly similar deformities if applied to the embryos at the same developmental stage. From the large, easily seen deformities resulting from severe or crude treatment, it follows that many pathologic conditions and subnormal nervous reactions are the result of unfavorable environments acting on the nervous system during development. These arrests probably make up the greater part of congenital nervous conditions, feeblemindedness and other conditions. Probably only a few such conditions are strictly speaking actually inherited per se, though this in no sense would indicate that they do not tend to recur in families. The excit-

ing cause itself may be associated with some hereditary structural condition, such as a poor uterine development and bad placentation due to weak or abnormal ovaries. This again shows how, in mammals at any rate, the glands of internal secretion may have something to do with malformations of the central nervous system, since they may effect the manner of placentation and thereby the supply of oxygen to the embryo and its rate of development.

DISCUSSION

DR. SMITH ELY JELLIFFE: Would it be valid to say that in the early linear stage of development we are concerned with the older phyletic system so that the lateral buds go through a separate development for the projicient system? I would also like to know whether the olfactory segments can be isolated. Can one draw any inference as to the development of the phyletic stage? Can one cut out the eighth nerve and eliminate the auditory and vestibular tracts which are of great importance in the projicient segments?

In another type of question, removed from the foregoing discussion, and relating to every-day matters, it is said that in the development of any series of segments there are times regulated by mitoses when certain effects can be produced. Has this any relation to the common statements in folklore regarding prenatal influences, which result in deformity to the child? We all know the common stories. A window drops on a pregnant woman's wrist, and her child is subsequently born without a thumb or with a stump for a wrist. There is the mass of contradictory evidence of other women who suffered the same accident and had normal children. Can this mean that in the first case the accident happened at a time when the finger buds were in active developmental stages of mitosis and thus sensitive to deforming effects?

In regard to the pigmental system: Can Dr. Stockard's remarks be said to extend to other types of pigment than the retinal pigmental system, such as the malpighian layer? In the rats which showed hemorrhagic spots of the skin what possible embryonic relations could that have to pigment layers of the eye? Is the whole pigment system in a class phyletically related to pigments of the eye? Or is it related to the older vegetative system?

DR. GREGORY STRAGNELL, by invitation: I should like to inquire about certain postnatal conditions which seem related to the points emphasized by Dr. Stockard. We encounter results which are not perhaps so marked as in prenatal interference, but are far more complex because they occur later. Clinically we see cases in which infections interfere with the normal development and growth of the child. In children between the ages of 6 and 10 years, at the time of secondary dentition, the enamel buds are interfered with. We also encounter precocious gonadal developments, such as pubertas praecox, due to endocrine interference, although we do not exactly know what its mechanism is. It is more intricate but it apparently resembles prenatal interference. This brings up the question of what part the endocrins play between the nervous system and the muscular and general development. Can we have any information as to what endocrine disturbances have been observed when chemical or mechanical interference took place in the development of the embryo?

DR. C. R. STOCKARD, closing: In regard to the vegetative nervous system, as contrasted with the the central nervous system, I think there is a little evidence that the early straight shaft might be looked on as vegetative rather than central. During the last two years interesting anatomic work, not yet published, has been done by Professor Edwin Smith of the University of London. He has shown that the vegetative system is in the central part of

the brain. All the other developments are secondary and grow into the central nervous system. The blood supply lies between the primary and secondary parts. Some years ago I thought the invertebrate nerves comprised the sympathetic system, but I am not of such an opinion now. The invertebrate system controls all kinds of muscles. Arthropods have striated muscle, and this looks more like the central nervous system than the involuntary system. I have not worked on the olfactory segment, but when you get cyclopia you get one naris. The auditory system is not strictly central nervous system. You can suppress the inner ear portion. Fishes do not have a middle ear, they have gills. The ampulla is first in the development of the cyst. You can get a big dilatation of the otic vesicle and fuse the ear right through the brain. The bony part of the middle ear will depend on the membranous labyrinth. If you transpiant otic tissue anywhere you will get a cartilaginous formation around it.

In regard to prenatal impressions: I do not think there is any evidence to connect these two things. You cannot associate the condition in the embryo with any accident to the mother, except in so far as shock to the mother will arrest development. I recall one case of an achondroplastic dwarf, called the "turtle baby" whose mother was said to have been badly frightened by a large turtle; but, as we know, achondroplasia is a hereditary condition, a true germinal mutation.

In regard to the pigmental system: The retinal pigment is different from the rest of the pigment. Other pigment is really mesenchymal, formed from migratory cells which become chromatophorous.

In reference to postnatal effect: I should have said that the further back you get in the embryo, the more fundamental the modifications are. You have the beginnings or "anlagen" as it were; later the effects are more complex. In regard to postnatal work: We must not regard birth as anything more than an accident in the development of the person. To say that the baby is increased by four times its weight after birth is nothing to the enormous increase, about 1,000 times, in the first nine months of its existence. The thymus cannot inhibit that growth, so that the endocrinal influence has definite limitations. In studying the question of growth we must look on life as a whole. Trees, for instance, show a steady generalized growth, but if they have glands of internal secretion we do not know what they are. The invertebrates reach a large growth, but they have no glands of internal secretion. The giant squid goes on growing as long as it lives; if you cut a limb off, it regenerates; and the same with amphibians. In the more complex organisms, the mammalian and avian embryos, there is another influence besides the older generalized power of growth. The egg increases 100 times, without differentiated glands, but when it reaches a certain stage it cannot do without the stimulus of internal secretion. The human baby cannot progress without the thyroid gland.

In the salamander, experiments were worked out with the attempt to bring about metamorphosis by addition of thyroid, but it was found that these creatures had a well-developed thyroid, and yet lived in the larval stage. The addition of hypophyseal secretion brought about metamorphosis. Thus it seems that the thyroid secretion could not become active without the pituitary. In the more complex stages of development the endocrine secretions become hooked up and interdependent. Until then the animal has the generalized power of growth. This stage is important in the development of the child as it influences the rate of oxidation and through this the determination of postnatal abnormalities. Interference always slows oxidation and retards the parts that should be developing rapidly.

An interesting phenomenon is seen in cattle with twins. This is rare, but when twins of the same sex occur, they are normal. When, however, there is one male and one female twin, the male twin develops the testicle before the female develops ovarian cells. The fluids of the male pass through the female. There being an arterial anastomosis of the two placentae the fluids pass through the two embryos. The female is born with defective sexual development. The male twin cannot be similarly affected, as it possesses an immunity to the maternal secretions. The hormones of the male differ from those of the female, and the egg which produces the male is different from that which produces the female. Thus it is seen that the glands of internal secretion begin to play a part at an early stage of development.

The Society adopted resolutions on the death of Dr. Pearce Bailey.

CHICAGO NEUROLOGICAL SOCIETY

Regular Meeting, March 16, 1922

CHARLES F. READ, M.D., *in the Chair*

A CASE OF INTENTION TREMOR AFTER ENCEPHALITIS APPARENTLY NOT OF THE EPIDEMIC TYPE. HUGH T. PATRICK.

A girl, 16 years old, was in good health until February, 1917, at which time she is said to have had scarlet fever and diphtheria. Antitoxin was given and there was a positive throat culture. After a few days of acute illness she developed marked shaking and tremor of the head and trunk, on a few occasions being thrown out of bed by the violent muscular contractions. About two or three weeks after the onset she remained for about a week with the eyes closed. Whether she had double ptosis or was partially unconscious is undetermined, but at the end of a week, when she opened her eyes, there was no strabismus and vision was unimpaired.

Following this there were three large abscesses in the back. She was in bed for three months and for six months was unable to stand or walk alone. Since then the condition has remained much as at present. When at rest nothing is to be observed except perhaps a lack of facial expression. She is quiet and comfortable. As soon as she begins to move marked tremor appears.

Apparently she had something like encephalitis almost two years before epidemic encephalitis appeared in this part of the country. The condition is like that presented by some patients following epidemic encephalitis. The intention tremor of the arms is not exceedingly marked, but any test will bring it out. As not infrequently in multiple sclerosis, tremor of the head and trunk shows very well when she walks and tests show marked intention tremor of the legs. She walks a little wide footed because the shaking affects equilibrium, but there is no real ataxia. Aside from this really typical general tremor, no ill effects are apparent from this acute illness, except that she is not able to wrinkle her brow or her nose. The pupils are not irregular, and respond to light and accommodation. She is intelligent and not nervous though somewhat sensitive. She has attended school and two years ago passed a written examination for which she had to be allowed additional time, but it was legible. There is no tendency to stammering though the tremor slightly affects her speech.

I have given scopolamin and belladonna, but with practically no effect. I shall next try gelsemium which Dr. Foster Kennedy has found useful in some cases of post-encephalitic tremor.

DISCUSSION

DR. SANGER BROWN: Many years ago Dr. Ringer reported many cases of tremor in which he thought he secured results from calabar bean.

DR. I. B. DIAMOND: I saw this patient when she had scarlet fever, at the time she was peeling. There was marked twitching of the body, and she could hardly be kept in bed. She is much better now. She was then emotional, excitable and greatly emaciated. I diagnosed the case as chorea and gave her arsenic.

A CASE OF UNUSUAL RIGIDITY FOLLOWING LETHARGIC ENCEPHALITIS. HUGH T. PATRICK.

This man, 36 years old, illustrates two features of epidemic encephalitis which we have learned to recognize during the last two or three years. In November, 1918, he suddenly became ill with fever, chills, considerable prostration, aching of the legs and excessive perspiration. He was in bed about a week, then gradually recovered and worked as usual ten hours a day for nearly a year, running a rip saw in a box factory.

After about eleven months, he had a severe headache one morning; in the afternoon he had to stop work. The headache continued for about four weeks, was frontal and quite severe. During this period he felt drowsy but could not sleep and had diplopia for about two weeks. Insomnia was extreme and hypnotics were deemed necessary for about three months. The insomnia gradually disappeared, but the patient felt prostrated, was without ambition and was unable to work for five months, when he resumed his former occupation but not with former strength and vitality. At this time the gait and movements of the extremities are said to have been normal. He continued work until October, 1921, but laid off for periods of one day to a week on account of general weakness. During the summer of 1921 his movements gradually became slower, more clumsy and more difficult. By October he was unable to work. His face became expressionless and speech slow, so that by the end of October a physician considered that he was mentally unsound. He was sent to the Psychopathic Hospital where he was found mentally intact and the real condition recognized.

At present the patient presents the picture of the parkinsonian type of postencephalitic condition. He has practically no tremor, but the so-called rigidity is marked to an unusual degree. Sometimes it is fully a minute before he can start a desired movement. This delay applies to all extremities but is exceedingly variable. This variability in motor capacity in this disease, as in dystonia musculorum and other extrapyramidal motor disorders, frequently has led to a diagnosis of functional disease.

A case similar to this but much more severe occurred in a lad of 15. For months the patient was supposed to have purely functional disorder, and I had him under observation for several weeks before I reached a definite diagnosis. In this case also the trouble steadily progressed for more than a year after the onset. At no time was there any paralysis, but the difficulty in initiating movement was so great that sometimes it took him three or four hours to eat a meal, and at times two or three hours to put on one or two garments. On one occasion, when the bowels were loose, he succeeded in reaching the toilet, but having arrived there could not turn around to seat himself in time to avoid an accident.

DISCUSSION

DR. A. B. YUDELSON: Have you observed that when these patients are asked to do something with their arms in adduction they can do it more readily and there is less tremor than when they execute an act with the arms in abduction, away from the body? I have observed this phenomenon in several cases examined.

DR. PATRICK: I never have.

DR. G. B. HASSIN: I wish to call attention to the anatomic changes assumed to be responsible for the clinical symptoms in the two cases presented. The choreiform movements and tremor of the girl are most likely due to a lesion of the corpus striatum, while the rigidity, masklike face and the slowness of movements so well shown by the other patient indicate, according to some investigators (Foerster, C. and O. Vogt and others), a globus pallidus lesion. The anatomic designation would seem more appropriate, for by using the terms pallidal or striatal syndromes we do not commit ourselves to the etiologic factors, such as syphilis, arteriosclerosis, inflammations, which all may cause lesions of the above structures and similar clinical pictures.

DR. J. ELLIOTT ROYER: The syndrome of the second case I believe is due to a bilateral lesion of the pallidal system: First, his rigidity is plastic or waxlike in character in contradistinction to the spastic and elastic type found in pyramidal tract lesions. Second, there is paralysis of automatic and associative movements with preservation of acquired or educational movements as shown when the patient wrote for us so well. It would appear that the motor system of the corpus striatum, the large pallidal cells, which have been shown to be the most essential lesion in the production of the syndrome of paralysis agitans, controls the automatic and associative movements and functions through the extrapyramidal motor tracts.

AN UNUSUAL CASE OF TABES WITH ARTHROPATHY OF THE SPINE. HUGH T. PATRICK.

The patient with tabes is unable to be present, because he suddenly became paraplegic following an intravenous injection of arsphenamin. He is a man 43 years old, whose family and previous history are of no particular importance except for gonorrhea twice at 25. He persistently denies chancre but has a cicatrix on the penis. For a number of years apparently he had some rheumatism, but the tabes probably began four or five years ago with rather typical pains in the legs. He went the course of the ordinary nonataxic tabetic, except for enormous loss of weight without any known cause. He had weighed when well 268 pounds (121.5 kg.), and in the course of four or five years he went down to 134 pounds (60.7 kg.) and less, about half his former weight.

The next interesting feature is flaccid palsy of the peroneal group of muscles of the right leg with foot-drop and marked atrophy. There is also some wasting of the right calf and thigh. Such palsies in the course of tabes have often been described, especially by Déjerine and his pupils. Occasionally they add difficulty to the diagnosis. Evidently the lesion is in the anterior horn, the anterior roots or the nerve trunk.

The third feature of note is that results of examination of the blood and spinal fluid by different men have always been negative.

Fourth, the patient has a knuckle of kyphosis involving especially the first lumbar and last dorsal, and roentgenograms show distinct lesions of the bodies of two vertebrae, with practical collapse of one and detritus about them. This lesion is painless and not tender to pressure either vertical or lateral, but heavy

percussion (fist) over it causes a shooting pain into the left thigh. At this time I cannot positively exclude tuberculosis, but everything points to tabetic arthropathy.

Is the atrophic, flaccid paralysis due to the bone lesion? I think it unlikely. Such palsies are exceedingly rare in spinal arthropathy, and in the vast majority of paralytic cases no bone lesion has been present. If the paralysis were due to involvement of the nerve roots by the bone lesion, one would expect pain and probably pain with anesthesia in the peroneal region. These sensory symptoms are not present. Nor are there other symptoms indicating involvement of the cord or cauda equina at the level of the spinal lesion.

Aside from the negative serologic findings and the absence of ataxia, practically all indications of tabes are present. The pupils are irregular, unequal and with the Argyll Robertson sign. The knee reflexes are absent, the left Achilles reflex is good, on the right not to be obtained. There is analgesia of the ulnar trunk, testicular analgesia and a zone of trunk anesthesia, wider for touch than for pain; also some analgesia of the legs. The shooting pains are quite typical.

DISCUSSION

Dr. James C. Gill: Was there any disturbance of the upper extremities?

Dr. Patrick: Practically none.

Note: This patient was seen again April 2. The paraplegia had largely disappeared and his condition was much as before except that flexion of the left thigh was feeble. Apparently the paraplegia had been due to a moderate Herxheimer reaction, although an acute exacerbation of tabes, such as reported by Dr. Holmes at the last meeting of this Society, could scarcely be excluded.

A CASE OF TABES WITH ARTHROPATHY OF THE SPINE. William H. Holmes.

C. W. (Case No. 97514), a white man, aged 52 years, was admitted to Wesley Memorial Hospital, Feb. 24, 1922. He complained of urinary incontinence, difficulty in walking and intolerable pain in both lower extremities. His family and early personal history was negative except that he had a double venereal infection twenty-two years ago and a serious accident twenty years ago, which may have a bearing on his present condition. The wire cables used in hoisting a steel girder parted, the girder fell, pinning the patient between it and another girder. He sustained a serious fracture of the right shoulder and contusions of the neck, chest, right arm and lumbar spine.

Immediately after the accident he experienced difficulty in controlling his urine, which has persisted to the present time. No attention was paid to the injury of the back which was regarded as unimportant. Ten years ago while employed in a position which required the lifting of heavy objects he suffered pain in the lumbar region. Aside from this short period there has been no disability because of backache. About five years ago severe lancinating pains in the abdomen and legs and nausea and vomiting began. A diagnosis of duodenal ulcer was made and an operation was performed. No evidence of ulcer or other abdominal disease was found, and reexamination resulted in a diagnosis of tabes dorsalis. Five weeks prior to his recent admission to the hospital there was a recurrence of lightning-like pains in both legs and in addition a more or less constant pain limited to the dermatomic distribution of the right fourth lumbar nerve. This pain sometimes disappeared on changes in position, more especially by flexing the spine and by reclining on the right side with the knees drawn up.

On recent admission to the hospital examination revealed all the classical symptoms of tabes. The right leg from a point just below the knee to a point just below the ankle on the inner surface was hyperesthetic and corresponded to the area in which the patient experienced pain. The tabes did not seem satisfactorily to explain the constancy of one type of pain in a limited area which could be alleviated by changes in posture. Examination revealed absence of the normal lumbar curve. The spinous process of the third lumbar vertebra was unusually prominent. Deep percussion did not cause pain. There was no muscle rigidity. Flexion of the spine was performed without difficulty. Rotation movements and lateral bending to the right were also well performed. Lateral bending to the left was limited and extension movements of the spine were quite impossible because of fixation and not because of muscle rigidity or pain. An antero-posterior roentgen-ray view of the spine in the lumbar region shows extensive deposits of new bone involving all the lumbar vertebrae with the most marked change in the second. There is marked lipping of the third, fourth and fifth vertebrae. When discharged from the hospital on February 27, his physician was advised to produce immobilization of the spine in extension by means of a plaster body cast.

DISCUSSION

Dr. Peter Bassoe: I might mention a case somewhat similar to the one reported by Dr. Patrick, with foot-drop, which shows that we should not be so pessimistic regarding therapeutic results. Ten years ago I saw an apparently hopeless case of what may be called paralytic tabes. The man had had tabes for many years with so much pain that he was addicted to opiates. He was lying down practically all the time and could not walk. He had optic atrophy, and foot-drop on the right side. He had a marked deformity of the lower lumbar spine, a marked prominence and hypermotility so that there was a grating sound when he moved his back. This did not cause any pain, and it was plainly a Charcot spine. Roentgen-ray examination showed that the fourth or fifth lumbar vertebrae were greatly affected.

I began treatment with mercury and then gave arsphenamin, but something peculiar happened: he received Swift-Ellis treatments and after one he suddenly developed left foot-drop. This came on like a Herxheimer reaction, and continued for some time but improved steadily. In a general way also he improved. Dr. Ridlon saw him and applied a spinal jacket. The man has continued to improve and is able to go to business. He walks poorly but can get out and into an automobile, go to his work and stay there all day. He is practically free from pain and has gained much in weight and general health.

I think the foot-drop in that case must be considered to be connected with the deformity, perhaps by traction on the cauda equina.

Within two days of the time I saw that case I saw another—that of a tabetic with great pain and bladder disturbance who also had arthropathy, but without much deformity or difficulty in locomotion. He soon developed pneumonia and died.

Dr. Elven J. Berkheiser: Dr. Ridlon has taken care of patients with these cases which are not so uncommon, as Dr. Funston of Iowa City, in a recent report in *The Journal of the American Medical Association*, would have us believe. Dr. Ridlon remembers four such cases. He emphasizes some points in the orthopedic treatment.

In one of his earlier cases he used a spinal brace to relieve the symptoms and prevent increase of the deformity. Little relief was obtained. In another case the patient was a large man who did hard work. A leather jacket was applied, which when new gave relief, but after it had been worn for a long time and became soaked with sweat it lost its shape and the symptoms recurred on account of the lack of proper support.

The two other patients have been relieved of symptoms by wearing a jacket made over a corrected torso. One has been wearing such a jacket for eight years. At first he had a great deal of discomfort, disability and paresthesia and was scarcely able to get about. After making an ordinary plaster form of this person, filling it with plaster and correcting this so that there would be some pressure on the convexities and room over the concavities, the man has been very comfortable and there has been no increase of deformity.

CASE OF MYOTONIA ACQUISITA. Lewis J. Pollock.

A woman, 29 years old, has been married for seven years and has had three children. Following the birth of the second child, four years ago, she awakened on the fifth day with her arms and forearms spasmodically flexed and her hands semiclenched. She was unable to overcome the contraction, but I have been unable to determine whether the spasms were paroxysmal or continuous. Six months after the onset they were definitely more or less constant, and at this time affected the lower extremities as well as the upper. In addition to the constant hypertonicity there were spasms which appeared at the beginning of any intended movement and diminished with each succeeding one. During the last two years the disease has been almost stationary.

An examination revealed a more or less constant spasm in the legs, producing bilateral hammer toes, and a rigidity of the feet which it was difficult to affect by passive movements. There was marked hypertrophy of the muscles of the legs. In the upper extremities there was marked hypertrophy of the deltoid and particularly of the muscles of the forearm. The hands were held in a position of ulnar deflection with the thumbs extended and the fingers flexed at the metacarpophalangeal joints. The arms were adducted and the forearms flexed to a right angle. Passive movements of the upper extremity were difficult. Following deep pressure over the biceps and deltoid muscles a groove was formed from which a slow wave of contraction of the muscle was seen. There was an increase in the idiomuscular reflex in the deltoid. Voluntary closure and opening of the hands was accomplished at first with great difficulty which became less with each succeeding trial. In the lower extremities relaxation did not follow successive movements.

There was no Trousseau or Chvostek sign. Electrical examination did not reveal a true myotonic reaction. It was observed that after the normal, quick response to cathodal closing stimulation there occurred a slow, tetanic spasm of the extremity, which did not correspond to the contraction of a group of muscles supplied by any one nerve. To faradism the reaction was normal.

Myotonia acquisita occurs as a complication of a number of diseases, such as syringomyelia, certain types of progressive muscular dystrophy and atrophy. In some cases of tetany myotonic phenomena have been present. Schiefferdecker and Schultze, in discussing tetany with myotonic phenomena, reported a case of gastric tetany with Trousseau's sign but no Chvostek sign, in which a long lasting after-contraction was present in a muscle after percussion. Schultze, in 1882, had already called attention to the intention spasm in tetany,

reporting two cases. Frankl-Hochwart, in 1891, cited two cases, one showing a Trousseau but no Chvostek sign. Kasparek reported a case of tetany with intention spasm, as did Hoffman. Bettman reported a case of Thomsen's disease with tetany and Trousseau's sign; after two years the tetany disappeared, but the myotonia remained. Von Voss described a case of tetany with myotonic disturbance and recalled the observation of Koester, who observed myotonic spasms in a case with irregular localized tetany.

My case shows phenomena which occur in both tetany and myotonia. The onset following pregnancy, the continued spasm of sudden onset and the position of the hands and feet indicate tetany. The presence of marked muscular hypertrophy, increased idiomuscular reflex and intention spasms indicate myotonia. I am inclined to classify this case as an atypical, chronic tetany with myotonia.

DISCUSSION

DR. E. B. YUDELSON: Were the ocular movements normal?

DR. POLLOCK: There was no change in the ocular movements. There was no discernible change in the thyroid. Metabolic studies revealed nothing definite. I administered parathyroid gland, and she immediately became worse.

DR. H. I. DAVIS: Was her breathing normal?

DR. POLLOCK: Perfectly normal. I think the tetany was probably related to the puerperium. As myotonic reactions have not been infrequently described, I would say that the same toxic factor which produces the tetany might produce the myotonia.

Book Reviews

L'ENCÉPHALITE LÉTHARGIQUE. Par le Pr. Achard, Professeur de Clinique Médicale a la Faculté de Médecine de Paris. Paper. Price, 16 francs. Pp. 324, with 15 illustrations. Paris: Librarie J.-B. Baillière et Fils, 1921.

The author goes back to a description by Camerarius of an epidemic in Tübingen in 1720 of what was called sleep sickness, and he believes that more careful research would bring to light much older records of like events. Indeed, reference is made to a number of much older statements which may perhaps have related to lethargic encephalitis. From these early indications the history is traced to and through the manifestations of the late epidemic.

The description of this polymorphous disease is full and accurate, the vastly different types being sufficiently emphasized. The pathologic anatomy is clearly presented and an attempt made to correlate the lesions of different parts of the central nervous system with the various symptoms.

Epidemiology, etiology and the relation of lethargic encephalitis to other diseases are duly considered, followed by diagnosis, prognosis and treatment. One could wish for more detailed information on prognosis but perhaps at the time the manuscript was finished, the author had not yet seen the manifold relics of the disease which have been so ubiquitous in the last couple of years and which give the prognosis such a somber cast. Recrudescence or return of progressive symptoms receives definite notice.

The entire monograph is good and constitutes a satisfactory, systematic treatise on this exceedingly important disease. The bibliography is extensive (about a thousand references), and should be most helpful to any one looking up the literature. The illustrations are well chosen, and the book (paper bound) is well printed on good paper.

AN ESSAY ON THE PHYSIOLOGY OF MIND. An Interpretation Based on Biological, Morphological, Physical and Chemical Considerations. By Francis X. Dercum, A.M., M.D., Ph.D., Professor of Nervous and Mental Diseases in the Jefferson Medical College. Cloth. Price, $1.75 net. Pp. 150. Philadelphia: W. B. Saunders Company, 1922.

This small volume, as indicated by the subtitle, deals with the mechanisms of neuron activity as applied to the study of human behavior. It is admirably written and makes excellent use of the work of Parker, Herrick and Sherrington. As a mechanistic foundation for the study of mental activities it contains much of value, even though the title is in some respects misleading. The author is deeply impressed with the conception that "mental phenomena are in their essence physical," and he carefully omits consideration of the dynamic factors which differentiate living from nonliving matter. Much is said of the influence of external "impacts" and their mode of transmission from receptor to effector, but the forces inherent in life, which surely are important determinants in the selection of reactions to these impacts and thus to self and race preservation, are almost entirely ignored. That such forces, primarily unconscious, may be the origin from which are evolved the mysterious instincts, feelings, desires and will is not considered.

As a direct consequence of this studied avoidence of the dynamic aspects of mind, instincts and affects are briefly mentioned, and the explanation is given that "a detailed consideration of the affective qualities of mind would lead us too far afield." But even here the author does not refrain from suggesting that, in the *production* of affects, "the internal secretions, the hormones, and the sympathetic and autonomic nervous system play an important part; at times the active cause is to be sought in toxic substances bred within the body or taken in from without." Melancholia and mania are cited as affective upsets with the somewhat naive suggestion that blocking of a synapse by toxic action "may itself be cause of pain *in the neurone*" (italics by reviewer) and that the "expansion" of the manic may be due to "the general release of inhibition" by toxic damage of synapses.

In dealing with the evolution of the nervous system and the development of associative chains of neurons, in discussing consciousness and its relations to neuron activity in the telencephalon and to "adjustable" as opposed to automatic or fixed responses, the author is on safe ground and handles his material ably. But even here, unfortunately, he is at considerable pains to brush aside the need for recognizing any vital force "an immaterial something of unknown and unascertainable character." He offers instead descriptive concepts such as chemotaxis, neurobiotaxis and ameboid activity of neurons which are in some way activated by external impacts, and one is left to wonder why evolution occurs at all.

That it is the purpose of the author to offer explanations of behavior rather than simply to describe the mechanisms through which this is manifested, is proved conclusively by the "addendum on pathologic physiology of mind" which occupies the last sixteen pages of the book. We can agree heartily with Dr. Dercum that there is urgent need for the student of mental activities and disorders to keep his feet solidly on the rock of observable fact, undoubtedly the main reason for the writing of this book, but surely it is just as unscientific to fight against the recognition of unknowable forces and their effects in biology as it would be to deny the force of gravity in the study of physics. The deletion of desires and affects makes of behavior a dynamo without magnetism, a lifeless mechanism which cannot be vitalized even by the most ingenious hypotheses of chemistry or physics. Unfortunately the elimination of this force is the keynote of the book and thus seriously mars the good qualities it possesses.

LA REACTION DU BENJOIN COLLOIDAL ET LES REACTIONS COLLOIDALES DU LIQUIDE CEPHALO-RACHIDIEN. Par Georges Guillain, Professeur agrégè à Faculté de Médecine de Paris, Guy Laroche, Médecin des Hôpitaux de Paris, et P. Lechelle, Ancien interne des Hôpitaux de Paris. Paper. Price, 12 francs net. Pp. 146, with illustrations. Paris: Masson et Cie, 1922.

As the authors of this little monograph point out, several attempts have been made to find a test for the study of variations in the cerebrospinal fluid, especially in syphilitic conditions, which may be used either as a substitute for the Wassermann test or as an adjunct to it. The most important of these is, of course, the Lange colloidal gold test, which is excellent and usually satisfactory, but which often leads to erroneous results owing to the fact that the solution is improperly prepared or is not stabilized. The mastic reaction of Emanuel has not proved sufficiently uniform in its results to warrant its

adoption, while the Berlin blue test of Kirchberg does not give typical precipitation curves, although it may show an intensity somewhat proportional to the increase in protein bodies.

The authors experimented with a large number of colloidal solutions until they finally adopted a colloidal suspension of benzoin resin. This test is based on the fact that colloidal suspensions of benzoin resin tend to flocculate and sediment out in proportion to the amount of protein, especially the globulin element of the spinal fluid to which they are added. As a test solution the authors use a colloidal suspension of the amygdaloid Sumatra benzoin.

In nonsyphilitic diseases of the nervous system, the authors assert the result is always negative. They made tests in cases of dementia praecox, old melancholic states, manic-depressive psychosis, alcoholic psychosis, morphinomania, cocainomania, uremic coma, arteriosclerotic hemiplegia, pseudobulbar paralysis, Parkinson's syndrome, chorea, amyotrophic lateral sclerosis, syringomyelia, paraplegia of old age and other conditions.

With different clinical forms of cerebrospinal syphilis the reactions are positive but vary in degree and somewhat in type. (1) In general paralysis the test is quite strongly positive and parallels the Wassermann and Lange tests. (2) In tabes this reaction presents different degrees of intensity which have some value in judging of the activity of the process. In progressive developing tabes it is as marked in some cases as in general paralysis, while in others it is less intense. In fixed tabes the reaction assumes the subpositive type, while in very old tabes the reaction may be negative. (3) In acute or subacute cerebrospinal syphilis, this reaction is positive, the precipitation occurring in the syphilitic zone. When the evolutionary syphilitic processes have ceased and such conditions as hemiplegia, monoplegia and paraplegia arise, the reaction is most often negative; in other words, the test in its positive phase has a definite relation to developing syphilis and not to the remote consequences of such conditions. (4) In the course of secondary syphilis, which is not associated with definite meningeal involvement but with slight lymphocytosis and a small degree of hyperalbuminosis, the benzoin test is negative. When, however, the Wassermann test is strongly positive and the lymphocytosis and hyperalbuminosis are distinct, the benzoin test assumes either the subpositive or positive phase. The authors classify the lesions of secondary syphilis into four groups: (*a*) Those showing no meningitic reactions; (*b*) those having slight meningitic reactions with weak lymphocytosis and hyperalbuminosis and with negative Wassermann and benzoin tests; (*c*) those with more marked hyperalbuminosis and lymphocytosis but still with negative Wassermann and benzoin tests, and (*d*) those with marked hyperalbuminosis and lymphocytosis and with a positive Wassermann reaction and a positive or subpositive benzoin test. Patients with secondary or tertiary syphilis with intense meningeal reactions may show just as strongly positive results as do patients with general paralysis or tabes; that is, this benzoin test is a syphilitic reaction of the cerebrospinal system and not a test of the type of syphilis. The benzoin test, according to the authors, parallels the Wassermann test in general paralysis and in active tabes; in fixed tabes the parallelism exists in most cases but there are occasional divergences. In acquired cerebrospinal syphilis, variable results have been reported, in some cases the Wassermann test being positive and the benzoin negative, while in others the reverse is true; but such variations are relatively infrequent. In all cases studied by these authors, as well as in analysis of reports of others, the Wassermann and benzoin tests were simultaneously positive in 83 per cent. of cases with a

variation in 17 per cent., of which 11 per cent. showed a positive Wassermann and a negative benzoin test and 6 per cent. showed a negative Wassermann and a positive benzoin test. These two reactions appear to be complementary, the benzoin test directing the diagnosis to a cerebrospinal syphilis while the Wassermann test appears secondarily after reactivation by treatment.

This test cannot be applied to cerebrospinal fluids which are purulent, turbid or contain blood or derivatives of it (xanthrochromatic fluids).

While the test has been favorably reported on by many writers, there are a few who doubt its value as a substitute for the Lange test. However, the results seem to parallel those of the Wassermann test in as large a percentage of cases as do those of other tests, and the preparation of the colloidal solution is much simpler and more constant than is that of the Lange test. The reviewer, from his experience with the colloidal benzoin test in his own laboratory, can recommend its use as an adjunct to the Wassermann reaction and believes that it will be found to be quite as reliable as the Lange test, especially if proper care be exercised in obtaining the amygdaloid variety of benzoin as advocated by the originators of the test.

Details of technic and guidance in interpretation are fully given in the monograph.